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TUBERCULOSIS

Clinical Aspects,
Prevention and Treatment

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TRANSLATED FROM THE RUSSIAN
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DESIGNED BY V. AN

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FOREWORD

The control of tuberculosis has entered a new stage. Highly effective means of prevention and therapy have become widely available, which is especially true under the Public Health system in the Soviet Union. There are now real possibilities for the total eradication of tuberculosis in the U.S.S R.

The present book contains a summary of modern knowledge on the clinical aspects and prevention of pulmonary and extrapulmonary tuberculosis and an outline of the latest developments in its therapy.

In a brief textbook, it is impossible and virtually unnecessary to present the detailed knowledge essential to specialists whose needs are amply met by other manuals and handbooks. The author's sole object is to assist the medical student and young physician in grasping the fundamentals of measures against tuberculosis and to explain how it can be prevented and successfully treated.

In almost 90 per cent of cases tuberculosis affects the lungs, such patients being the most dangerous source of infection for other people. Hence, the major part of the textbook is devoted to pulmonary tuberculosis. But as tuberculosis is a general disease of the human body, an understanding of its clinical features requires a knowledge of the tuberculous lesions afflicting other organs. Accordingly, the chapters on pathogenesis and clinical aspects include general information on skeletal and other localisations of the tuberculous process. However, within the confines of a brief textbook, we find it impracticable to deal with bone-and-joint tuberculosis, which is taught at the surgical departments of medical institutes and requires special knowledge of orthopedics and surgery.

V. Einis

INTRODUCTION

HISTORY OF RESEARCH

Tuberculosis has been known for thousands of years. In the words of the French medical historians A. Piéry and J. Roshem, it is as old as man himself. Thus, the earliest archeological discoveries of tuberculosis-like spinal lesions date back to the Stone Age. Vivid descriptions of the symptoms of "lung consumption" were left by the ancient Indians and Egyptians. The Indians held it to be an "evil" disease (Manu's law), while the ancient Egyptians, according to Isocrates, had already devised preventive measures and were long considered the most healthy and robust of nations. Hippocrates (Cos school, 460-400 B C.) was acquainted with pictures of "lung consumption" and attempted to treat the disease. The physicians of ancient Greece treated consumption in its chronic and acute forms, prescribing specific hygienic measures and regular diet, etc. The ancient Chinese were also familiar with tuberculosis and its symptoms, a description of which may be found in Chinese medical manuscripts, such as the treatise on medicine by Wang Shu-huo (6th century B.C.). Avicenna (Abu-ibn-Sina) in his *Canon of Medical Science* gives an interesting account of the heredity of consumption, the frequency of hemoptysis in spring, consumption in pregnancy, etc. The famous scientist also dealt with the effects of environment, climate and weather on the course of the disease.

Conjectures as to the infective nature of tuberculosis were advanced more or less definitely in the middle of the sixteenth century. Almost three centuries before Pasteur and Koch, Geronimo Fracastoro (1483-1553) of Verona persistently referred to its contagiousness. This view was gradually accepted by physicians, although there were some who denied it even in the eighteenth century.

The first mention of tuberculosis in Russia occurred in the fourteenth century, when the disease was called "malignant tabes" and "intractable ulcer".

During the Renaissance, in the fifteenth and sixteenth centuries, emphasis was placed on hygienic and dietary principles of treatment and climate therapy, although the current views on the disease proper were still rather rudimentary Some very interesting data were recently found by M. L. Goldfarb and A. V. Prussak in mid-seventeenth

century medical manuscripts. Apparently tuberculosis was then already widespread and considered as contagious as measles and smallpox. Only in the late eighteenth and early nineteenth centuries Bayle (1810) spoke of lung consumption as a specific disease springing from a tubercular lesion, for the first time distinguishing the miliary form. But of course, it is Laennec alone (1781-1826) who can claim the credit for establishing the specificity and single origin of the various clinical manifestations and stethacoustic symptoms of the disease. Later, in the middle of the nineteenth century, N. I. Pirogov described the clinical picture and pathological anatomy of acute primary generalised tuberculosis. In addition, he gave a clinical description of tuberculosis of the lungs, bones and joints, cerebral membranes, and lymph nodes.

The middle of the nineteenth century was marked by another development, viz., experimental proof of the infectious nature of the disease by Villemin (1827-1892). In 1855, he demonstrated that human tuberculosis could be induced in animals. Villemin asserted that the disease was caused by a live parasite existing and reproducing within the body and resembling the organisms which Pasteur had discovered to be responsible for fermentation. But this remained a mere conjecture until in 1882 the German scientist Robert Koch discovered the causative agent of tuberculosis—the tubercle bacillus or *Mycobacterium tuberculosis,* definitively proving it to be the only cause of the disease contained in tuberculous sputum, scrofulous lymph nodes, cold abscesses, etc.

This discovery was an irrefutable confirmation of Villemin's surmise, laying the basis of contemporary epidemiological and clinical research on tuberculosis and extensive experimental studies which gave rise to the modern concept of immunity in tuberculosis, of which Koch himself had furnished ample evidence. The immediate result of his discovery was the development of more rational preventive techniques for tuberculosis, a disease, it is relevant to recall, which at that time claimed the life of one person in every seven (R. Koch).

For some time, however, Koch's discovery minimised the importance of assaying resistance in tuberculosis. Only in the twentieth century (G. A. Zakharyin and A. A. Ostroumov et al.) and especially in recent years, has the problem of resistance at infection and during disease been given adequate attention, which was stimulated by the wider acceptance of the notion of tuberculosis as a general infectious disease.

The twentieth century has witnessed enormous progress in tuberculosis research. The pathogenesis and clinical features of pulmonary and extrapulmonary tuberculosis have been studied in great detail. The most significant advance was the new concept of tuberculous pathogenesis which succeeded the earlier notion of the obligate development of the process from the apex downwards. This, together with

profound studies of different forms, furnished the premises for new achievements in therapy.

Apart from pathoanatomic research, the modern concept of tuberculous pathogenesis owes its origin to the introduction of radiological techniques into clinical practice.

As a result of classic investigations with tuberculin—a glycerin extract of bouillon cultures of *Mycobacterium tuberculosis* discovered by Koch—Clemens Pirquet (1907) proposed the tuberculin skin test as a more or less precise means of diagnosis and helped to establish the regularities governing the length of incubation (3 to 8 weeks) and the changes of body reaction in tuberculosis. Pirquet discovered the phenomenon of tuberculous allergy, which plays an essential part in diagnosis and treatment, representing one of the major formative factors in various tuberculous manifestations.

Unfortunately, tuberculosis therapy made very slow progress. During the Renaissance (15-16th centuries), Matteo Ferrari left detailed prescriptions for the treatment of tuberculous patients, envisaging individual hygienic and dietary measures. In the second half of the 19th century the physiological trend gained precedence in clinical research on tuberculosis. Thus, Brehmer was responsible for suggesting and applying sanatorium treatment (1859), which even today is one of the basic curative methods. Brehmer was the first to prove the possibility of curing pulmonary tuberculosis by means of rational hygienic and dietary measures.

Examining the physiological laws of resistance, G. A. Zakharyin, V. A. Vorobyov, T. P. Krasnobayev et al., correctly emphasised the importance of hygienic and dietary measures in the treatment of tuberculosis. In 1838, G. I. Sokolsky, a lecturer in the Moscow University, had already drawn attention to the fact that only a rational diet could interrupt the process. A monograph by the Polish doctor A. Sokolowsky in 1913 gave a fine clinical description of tuberculosis, likewise noting the importance of general supportive therapy.

This principle is just as valid today, especially considering the prophylactic orientation of Soviet medicine as a whole.

Along with hygienic and dietary treatment, the method of artificial pneumothorax proposed by Carlo Forlanini in 1892, began to find extensive practical application after 1894. In Russia, artificial pneumothorax was first employed therapeutically by A. N. Rubel and A. Y. Sternberg. Since 1912, intrapleural pneumolysis after Jacobaeus gradually began to be applied in clinical practice to compensate for unsuccessful pneumothorax. Later, increasing use was made of extrapleural surgical interventions, such as thoracoplasty (Brauer, Sauerbruch, N. G. Stoiko et al.), extrapleural pneumothorax, etc. The first pulmonary resection was made in 1933 for carcinoma, although as far back as 1905 F. R. Kiyevsky had presented a thesis at Petersburg University entitled *On the Theory of Pulmonary Resections.*

Today, lung resection is one of the basic surgical methods in otherwise intractable forms of pulmonary tuberculosis performed, of

course, on appropriate clinical indications. All these measures, however, are valid only under a strict hygienic and dietary regime instituted postoperatively.

The extensive use of radical surgery in tuberculosis, especially segmental and subsegmental resections, was made possible by one of the greatest achievements of modern medicine—etiotropic antibacterial therapy. The last two decades mark a new stage in the therapy of tuberculosis associated with the discovery and wide practical application of antibiotics (streptomycin, Selman Waksmann, 1944) and chemotherapy. The new achievements in chemotherapy ushered in the era of etiotropic therapy, creating new possibilities for early treatment. All clinical means used previously, e.g., gold salts, had purely local therapeutic effects on the tissues. Nevertheless, the new measures of treatment and prevention could not detract from the importance of the hygienic and dietary regime. Modern combined therapy ensures recovery in a great many tuberculous cases and will no doubt help in the rapid eradication of tuberculosis as a social disease, provided, of course, that the scope of preventive measures, sanitary and specific, will conform to modern requirements and theoretical knowledge.

Pre-revolutionary Russia had no antituberculosis organisation of any importance, except for the charity-supported *Antituberculosis League*. After the Great October Revolution the antituberculosis system initiated by the Soviet Government and led by N. A. Semashko, Z. P. Solovyov, V. A. Vorobyov, Y. G. Munblit and others, planned and carried out a variety of prophylactic measures. Its activities were mainly responsible for a sharp reduction of tuberculosis mortality and morbidity. The antituberculosis dispensary became the centre of all activities in the area under its supervision, carrying out the entire round of therapeutic and prophylactic measures. Apart from sanitary preventive measures and domestic and labour welfare activities, specific B.C.G. vaccination after Calmette and Guerin has been increasingly used since 1926, all newborn babies in the U.S.S.R. receiving it (see Chapter XI).

Extensive sanitary measures, particularly among children (most firmly advocated by A. A. Kissel), large-scale housing construction, 7- and 8-hour working days, annual holidays for all workers, free medical care and constantly rising standards of living have all contributed to the success of preventive and therapeutic measures carried out under the tuberculosis control programme.

The strictly scientific tuberculosis control system inaugurated in the world's first socialist society expanded continually. A new Soviet school of phthisiologists developed rapidly. A substantial number of physicians, scientists and public health workers concentrated on the fight against tuberculosis and the training of specialists. The new conditions produced new forms of control, also largely due to the efforts of such public bodies as domestic and labour welfare committees, organised special commissions in the local Soviets, etc.

Numerous hospitals and sanatoria were built along with a comprehensive system of prophylactic institutions for children. Extensive research was initiated, special tuberculosis research institutes being established and the theory of tuberculosis becoming a subject at higher medical institutions. All-Russian and subsequently All-Union conferences of phthisiologists began to be held.

In the light of the new targets facing the Soviet Public Health service, important practical measures are being put into effect, particularly among children. An extensive early casefinding programme has been elaborated and carried out. A new Soviet system of clinical treatment for tuberculosis has been developed. The plans of the Soviet Government and Communist Party are being implemented with unparalleled enthusiasm, the road being opened for the total eradication of tuberculosis in the U.S.S.R.

Fig. 1 *Mycobacterium tuberculosis* in optical microscopy
a–stained after Spengler, *b*–stained after Ziehl-Neelsen

CHAPTER I

TUBERCULOUS INFECTION AND BODY REACTION

CAUSATIVE AGENT

Mycobacterium tuberculosis, the infective agent of the disease, was discovered in 1882 by Robert Koch. The microbe is found in the sputum, urine or pus of man and animals affected with tuberculosis. Two types of *Mycobacterium tuberculosis*–human and bovine–are of practical importance. Other varieties, occurring in nature, e.g., the avian and cold-blooded types, play no significant part in human pathology.

Of late, the so-called atypical strains of acid-fast mycobacteria are attracting attention. But so far, no final conclusions as to their role in human pathology have been reached.

In all, four varieties of atypical mycobacteria are distinguished according to features of pigment formation and rate of growth.

Mycobacterium tuberculosis is an obligate aerobe widespread in human communities, breeding and surviving for long periods in dark and damp places. In direct sunlight, however, the bacteria perish in a matter of several hours. According to Koch, the bacilli are 5 times longer than they are wide, varying from 0.0015 to 0.0035 mm (1/4 to 1/2 of the diameter of an erythrocyte). In sputum samples they are found either as solitary specimens, or in clusters. The bacilli reproduce by transverse fission, forming peculiar cords in solid media (Figs. 1 and 2).

Originally, it was believed that there are filtrable forms of *Mycobacterium tuberculosis* (Fontes, 1910), a view at one time supported by Calmette who considered that the now known classic form of the tubercle bacillus represented the end-product of ultra-virus development. However, this theory has not yet been confirmed.

At present, the physico-chemical composition of *Mycobacterium tuberculosis* is pictured as follows. It includes the usual organic protoplasmic components, namely, lipids, polysaccharides, protein substances (tuberculoproteins, partly albumins and partly nucleoproteins) and inorganic substances (water 86 per cent, solid substances 3

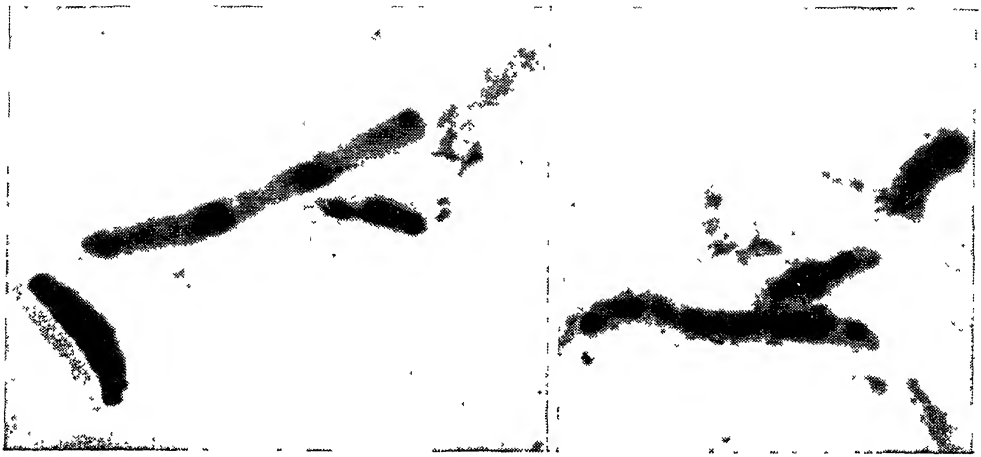

Fig. 2. Mycobacterium tuberculosis in electronic microscopy

Fig. 3. Corded *Mycobacterium tuberculosis* (microscopy)

per cent). Phosphorus, calcium, magnesium, and chlorine are the major elements accumulating in the bacillus body.

The protein components play a part in the sensitation of the macroorganism. When administered to infected animals, they elicit

anaphylactic effects similar to those of tuberculin. The lipids are often said to cause the formation of tuberculous tissue, in particular, epithelioid cells. The role of polysaccharides is not yet clear. It is believed that they are concerned with the development of immunity.

The action of these substances in the animal organism may be shown schematically as follows:

Tuberculoproteins → Antigen-antibody reaction → Initial lesion → Exudate

Tuberculolipids → Formation of epithelioid cells → Tubercle

Enough is now known of the ferment system responsible for the microbe's respiration and the ferments involved in the lysis of proteins, starch and fats.

The acid-fast tubercle bacilli are stained in preparations of sputum and other excreta by the conventional Ziehl–Neelsen method in which carbolfuchsin stains the microbes red, the background (cellular elements, detritus) being coloured blue by methylene (see Chapter V). It should be noted, however, that acid-fast saprophytes (*Bacillus smegmatis*, hay bacilli) stain similarly.

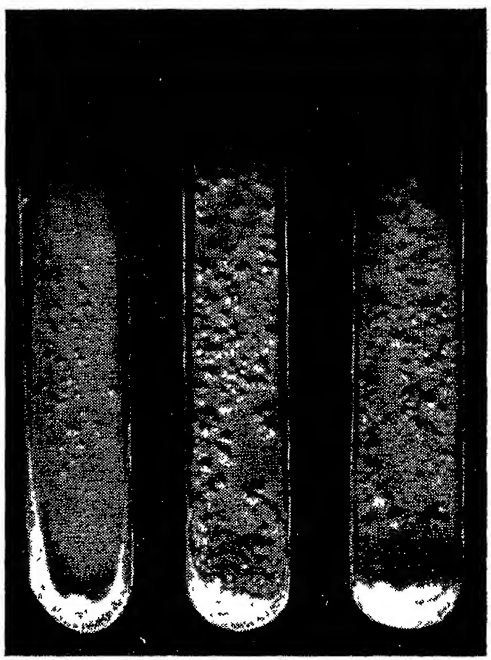

Fig. 4. Culture of *Mycobacterium tuberculosis* in solid egg medium

In doubtful cases, only cultivation of the sputum on special solid egg media or injection of bacilli-containing matter into guinea-pigs—animals highly sensitive to tuberculosis—may give a definite clue to the etiology of the disease. In positive cases, cultivation produces the typical growths of *Myco. tuberculosis* depicted in Figs. 3 and 4, which assume a characteristic cord-like shape. On necropsy, the viscera of tuberculous animals exhibit the characteristic tubercular rash or foci of caseous necrosis. It must be noted that after the introduction of isonicotinic acid hydrazides, mycobacterium strains resistant to these drugs are losing their virulence for guinea-pigs. In such cases, cultivation is the basic procedure to be used.

ROUTES OF INFECTION

Man most frequently receives the infection through the air, by inhalation. Incubation takes 3 to 8 weeks. In the aerogenous route, the infection may be conveyed by droplets or dust.

In the first instance, the tubercle bacilli, which are suspended in minute droplets spread by the patient while coughing or talking, are inhaled by the surrounding healthy people and may become the source of contagion. In the second, healthy individuals inhale dust in premises inhabited by tuberculous patients who disregard the common rules of hygiene. After drying, the drops of infected sputum form dust which may transfer from the floor, furniture and discarded handkerchiefs into the respiratory tracts of healthy people, especially children, and may become the source of infection.

Bruno Lange sprayed bacillus-containing sputum in droplets of varying size on woolen shawls. After drying for $1^1/_2$ to 24 hours, the contaminated shawls were brushed or shaken over a glass case. With low concentrations of tubercle bacilli in the original sputum, none of the exposed guinea-pigs contracted the disease. With medium concentrations, 3 out of 16 guinea-pigs were infected, while in 3 experiments with high concentrations, tuberculosis developed in 6 out of the 11 animals tested. This ratio is similarly observed in human communities. Thus, morbidity amongst the commensals of tuberculous cases is known to be considerably (3 to 4 times) higher than among the general population.

The possibility of contact infection, especially in childhood, naturally cannot be discounted either. Children touch the source of infection (handkerchiefs, crockery) with their hands, which thus become contaminated and, being applied to the mouth, nose and eyes, may cause infection. Contagion is likewise possible through ingestion of infected food, especially milk from cows with tuberculosis of the udder.

Instances are known of tubercle bacilli invading the body or being rubbed in through injured skin. In a case in the writer's experience, a laboratory worker fell ill after grazing his skin with an infected injection needle, a tuberculous papule developing at the site of invasion. Such cases are, of course, extremely rare.

The main source of human infection is inhalation, i.e., via the respiratory tract.

Of special practical importance today is the assessment of mycobacterial resistance towards the antibiotics (streptomycin, etc.) and synthetic drugs used in tuberculosis, primarily the isonicotinic acid hydrazides. Just as primary infection may be caused by resistant mycobacteria, so resistant strains unamenable to antibacterial drugs may emerge in chemotherapy, especially if it is unsystematic and inadequate.

INVASION. PRIMARY LESIONS IN THE LUNGS

Invasion usually takes place aerogenously. On surmounting the natural protective barriers and mechanisms, i.e., the obstacles encountered by the air in flowing through the convoluted upper respiratory passages (moving ciliary epithelium, muca), the tubercle bacilli penetrate with the air into the deeper sections of the respiratory tract. At the juncture between terminal and respiratory bronchioli (Braus's model, Fig. 5), or, according to N. F. Melnikov-Razvedenkov, at the site of physiological stenosis, a primary focus of tuberculous bronchopneumonia develops. Such a focus was described in 1912 by the Czech pathoanatomist Ghon. V. G. Shtefko observed primary lesions in the intestine in 12 per cent of all cases.

Most frequently the primary complex develops in childhood.

At first the pulmonary lesion presents a bronchopneumonia with rapidly necrotising fibrous-cellular exudate. A. I. Abrikosov distinguishes three phases in the development of the primary focus, viz., tuberculous pneumonia, caseous degeneration and incapsulation, calcification, or, occasionally, ossification, i.e., usually there is a tendency towards healing.

In a majority of cases, there is a single primary focus (according to V. G. Shtefko, in 83.5 per cent of all cases). Ghon observed several primary lesions in 16.5 per cent. In one exceptional case Ghon and Kudlich found 17 calcified foci in a three-and-a-half-year-old child. Literature on the subject indicates that on the average several primary foci are encountered in 12 per cent of all cases. As regards localisation, the primary lesion may be found in different sections of both lungs, in the right, however, more often than in the left. Apical localisation is rare.

As noted by Küss, primary lesions most frequently develop in pulmonary areas with intense ventilation, which apparently accounts for the usual subpleural localisation.

According to A. I. Abrikosov and A. I. Strukov, the size of the primary lesion varies from 0.5 to 2 cm and more in diameter. A caseous-pneumonic sequestrum in the stage of fibrous incapsulation is usually circular in shape (K. E. Ranke). A Ghon tubercle presents the pulmonary component of the primary tuberculous complex later described by Ranke. The second component of the complex is a similar type of tuberculous lesion in the regional lymph nodes.

Tuberculosis being a general infectious disease, a local pulmonary lesion is not the only change liable to develop in the body after invasion by tubercle bacilli. Apart from the described changes at the site of invasion and the occasionally observed dissemination through the viscera, the body as a whole responds to the invasion with what is known as allergy, which is revealed through the contemporary tuberculin reaction.

The human body offers adequate resistance to tuberculous infection. So, the pathological changes resulting from the primary infec-

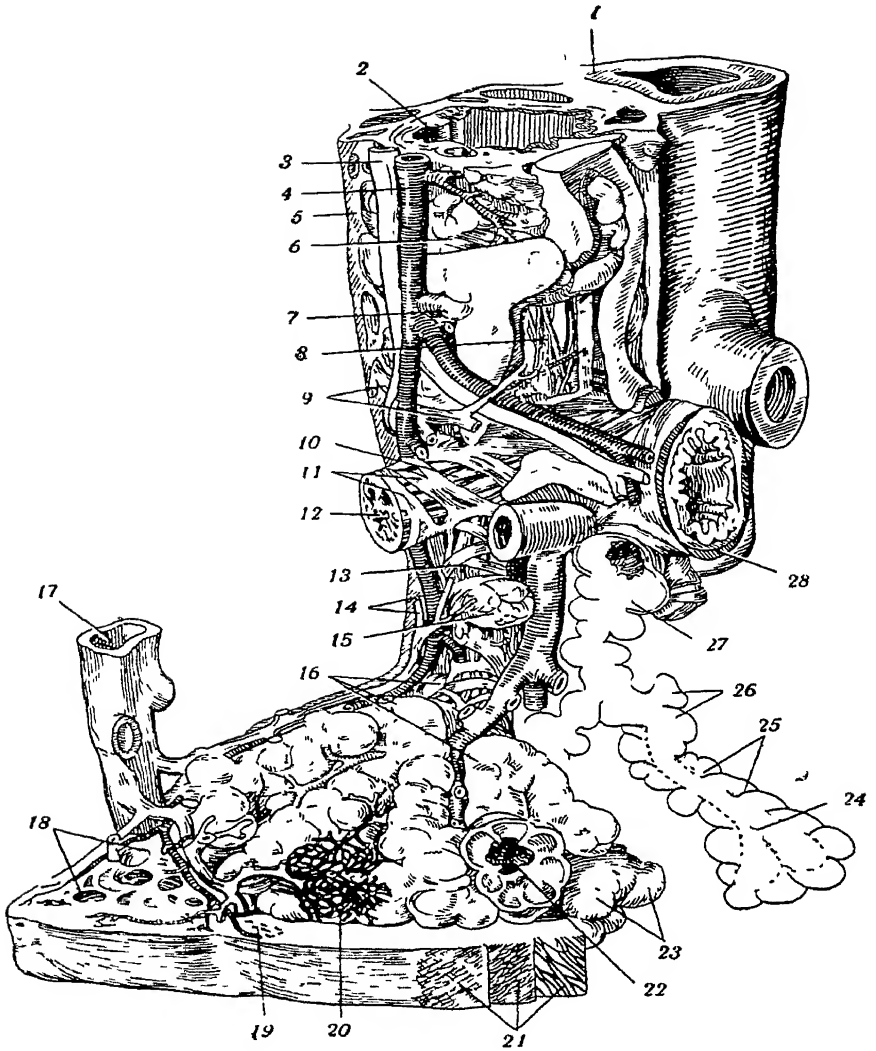

Fig. 5. Bronchial ramifications and structure of acinus (after Braus)

(1) pulmonary artery, (2) bronchial mucosa, (3) nerve, (4) bronchial artery, (5) connective tissue membrane, (6) muscular membrane, (7) layers of cartilage, (8) artificial aperture in muscular membrane showing elastic reticula, (9) bronchial veins, (10) network of elastic fibres, (11) network of muscular fibres; (12) bronchiole, (13) alveolar bronchiole, (14) bronchial veins, (15) alveole with elastic reticula, (16) three "atriums" of the alveolar tree, (17) pulmonary vein, (18) sinus of adjoining acinus (sectionalised), (19) pigment between acini, (20) alveolar capillary network, (21) three pleural layers, (22) alveolar sacs with alveolar apertures, (23) marginal alveoli, (24) alveolar passageway (with ramified end), (25) septa, (26) alveoli, (27) atrium, (28) bronchus

tion in most cases heal without resort to special measures. But when, subsequently, the disease develops in adults, it usually assumes a chronic course.

ALLERGY AND IMMUNITY

The natural resistance to tuberculous infection displayed by the human body forms the basis of the specific bodily response evinced at the invasion of tubercle bacilli (normergy). Clemens Pirquet proposed the term allergy* for this change in body reaction, which may assume different degrees of intensity. Thus, along with normergy, we may observe pathergy. At sharp increases of sensitivity to tubercle bacilli and their metabolic products (and also, possibly, to the endotoxins released at their disintegration) we speak of hyperergy. A drastic reduction of specific resistance and body reaction is known as negative anergy, usually involving paralysis of the protective functions. One of the main symptoms of allergy is increased sensitivity to tuberculin, which according to Koch is a glycerin extract of a bouillon culture of *Mycobacterium tuberculosis.* Tuberculin has been likened to an incomplete antigen (hapten). When administered even in large doses to a healthy animal or man it causes no reaction. On the contrary, subcutaneous injection into a tuberculous animal or man even in small doses or low concentrations (e.g., 1:1,000,000) produces an intensive reaction of threefold nature: (a) general febrile; (b) focal, manifested by an increase of inflammatory processes in the tuberculous focus existing in the given organism, and (c) local, i.e., originating at the site of injection.

The so-called tuberculin test is commonly used to determine the intensity of body reaction. The original Koch test comprised subcutaneous injection of pure concentrated tuberculin (O.T.-old tuberculin). At present, however, old tuberculin has been almost completely abandoned in general practice, the Pirquet scarification test and the Mantoux intradermal test being the routine diagnostic procedures which we shall deal with later.

After a certain period following invasion, the negative tuberculin reaction undergoes what is known as tuberculin conversion—a change whereby it becomes positive. This feature of the response to tuberculin injection is utilised in diagnosing infection, which, as is commonly known, is accompanied by a specific skin allergy manifested in a papule and hyperemia.

In assaying the results of cutaneous and, especially, intradermal tuberculin tests, account should be taken of postvaccination allergy which in intradermal BCG is observed in almost 100 per cent of cases 1 to 3 months after vaccination. Allergy after enteral vaccination persists for 1.5 to 2 years, and after intradermal for 5 to 7 years.

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* From the Greek *allos*—other and *ergon*—effect.

But the reaction of the body to the invasion of tubercle bacilli is not confined to the emergence of allergy. It is also symptomatised by the development of specific immunity, admittedly not as stable as in other infections, e.g., smallpox or scarlet fever, but undoubtedly of importance in organising the protective powers. The manifestations of specific resistance to tuberculous infection are irregular, often wave-like, hypersensitivity with more acute symptoms of the disease alternating with less marked symptoms and vice versa. There is also a certain conformity between the extent of the general body reaction and the changes within the tuberculous focus. For instance, pneumonic infiltrative foci in the lungs usually develop alongside more pronounced increases of sensitivity (hyperergy, hypersensitation). Proliferative processes and quiescence are often observed together with a certain reduction of sensitivity, i.e., desensitation.

It should be noted that changes in the allergic response do not invariably run parallel to the immunity curve. This in particular prompted some authorities to regard allergy and immunity in tuberculosis as mutually unassociated biological phenomena. In the author's opinion, however, they should be regarded as a single entity, i.e., as two aspects of the fluctuations occurring in body resistance.

As mentioned earlier, the body reaction is observed to vary broadly in the course of tuberculosis. Rather popular at one time was the view held by K. E. Ranke that the primary invasion leading to the formation of the primary pneumoglandular complex is followed by the emergence of allergic symptoms (stage I) developing on the basis of increasing sensitivity, which is followed in its turn by a tendency towards dissemination of the infection (stage II—generalisation), and a final process involving the growth of immunity, in which tuberculosis, as it were, assumes the form of a local lesion in a single organ (stage III—isolated tubercles).

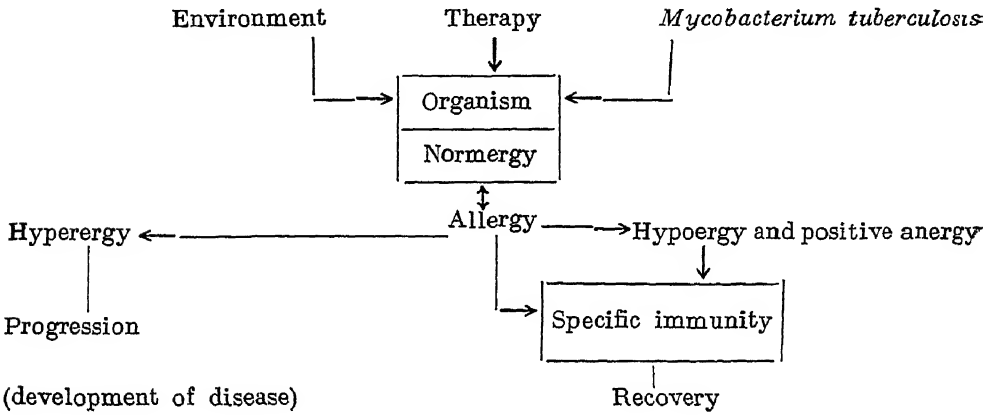
Ranke's views, however, met with serious clinical objections. Body reaction and fluctuations of the latter are associated not only with the tuberculous infection as such, but with all environmental factors affecting the patient. Thus, cases of localised or fixed pulmonary tuberculosis are often observed to exacerbate under various physical influences, e.g., the effects of solar radiation, continuous inadequate diet or intercurrent disease (after measles or whooping cough in children). In such cases the process is generalised hematogenously. In other words, stage III, as it were, is followed by a recurrence of stage II with high allergy and a tendency towards generalisation.

Sharp criticism of Ranke's theory together with subsequent clinical and pathoanatomical findings gave rise to the now commonly accepted division of the tuberculous process into two periods, viz., primary and post-primary or secondary, which will be described in a special chapter. Here it should be noted, however, that primary tuberculosis is mostly observed in childhood, although it is also encountered in

adults, especially today, when sanitary prophylaxis and preventive antituberculosis vaccination are transferring the incidence of tuberculous infection to later age groups.

Invasion and the subsequent development of the disease are thus accompanied by changes in the general body reaction and allergic fluctuations manifested in varying degrees of sensitation. The body responds to the primary invasion of the sensitising agent by a normergic reaction or euergy, i.e., "total physiological measures against the infection" (I. P. Pavlov), whereas repeated introduction of the same agent is followed by a pathologically changed reaction, or so-called allergy. Hyperergy, i.e., hypersensitation, is a term used to describe an acute (excessive) increase of sensitivity (see diagram).

Evolution of Reactions to Tuberculous Infection



In tuberculosis hyperergy assumes the form of intense exudative inflammation and a tendency towards necrosis. By positive anergy we presume a relative insensitivity towards repeated administration of tuberculin explained by the high level of the protective powers. Hence, rational therapy aims to normalise the pathologically changed reaction (the reactive powers, according to A. I. Abrikosov) by desensitation and by stimulating natural resistance and specific immunity.

Immunity is observed in people with a tuberculin-positive reaction. It is assumed to exist while living and virulent tubercle bacilli inhabit the body (non-sterile immunity). Occasionally, however, a different opinion is expressed. The introduction of dead bacilli into the animal body is also known to cause relative immunity. Hence, the so-called tuberculoid tissue is likewise an immunogenic factor.

The high degree of protective strength obtained through treatment and manifest in tissue immunity, leads to the intensification of healing processes in the foci of affected organs, resulting in the resorption

of inflammatory exudates, fibrous transformation of productive foci, healing of ulcerous lesions, and, in particular, healing and closure of tuberculous cavities. The changes which have been mentioned take place together with the total cessation of intoxication and normalisation of the metabolism, particularly oxidation processes. Sleep, appetite and body weight return to normal, and complete occupational rehabilitation ensues. Observing the recovery of tuberculous patients, one may remark the close connection between the general symptoms of the disease associated with disturbances resulting from toxicemic effects on the central and vegetative nervous systems and the condition of focal changes in various affected organs.

CHAPTER II

PATHOLOGICAL ANATOMY AND PATHOGENESIS

As mentioned earlier, tuberculous inflammation is caused by the invasion of tubercle bacilli which become lodged in various organs. The microbe acts as a foreign body, its metabolic products causing in the surrounding tissues an inflammatory reaction which includes specific and non-specific (paraspecific) components. The latter phenomenon is most vivid in primary pulmonary tuberculosis.

A prominent feature in the evolution of an inflammatory process, particularly exudative, is the tendency of inflammatory lesions to undergo caseous necrosis. For all the multiformity of pathoanatomical changes in tuberculosis, which may include alterative as well as exudative and productive processes, caseous necrosis is most characteristic of the evolution of tuberculous inflammation. The preponderance of one or another type of inflammation depends on the level of resistance in the given organism and will be described in appropriate subsequent sections.

PRIMARY COMPLEX IN THE LUNG

According to A. I. Abrikosov and A. I. Strukov, primary tuberculosis mostly occurs in childhood, but is also observed in adolescence (in 20 per cent of all cases) and even in adults (8 to 10 per cent).

A tuberculous focus appears at the site of invasion of tubercle bacilli in the pneumoparenchyma. The centre of such a focus presents an area of caseous bronchopneumonia. Initially, the perifocal area becomes the scene of non-specific serolymphocytic impregnation of tissues, otherwise known as perifocal inflammation. Since such a primary focus is always accompanied by lesions of the regional lymph nodes with more or less manifest caseous necrosis, there emerge, as it were, two poles of the inflammatory process connected by lymphangoitis, which are initially surrounded by an area of more or less vivid perifocal inflammation. Later, radioscopically, we may observe the gradual resorption of the perifocal inflammation, the described two poles of the inflammatory process becoming more

demonstrative (bipolar stage). The two extremes of the primary tuberculous complex are often clearly distinguished pathoanatomically (Fig. 6).

The initial stage in the development of a primary pulmonary focus is seldom detected. The earliest focus ever noticed was described by Ghon and Roman in a five-and-a-half-months old infant. In the first

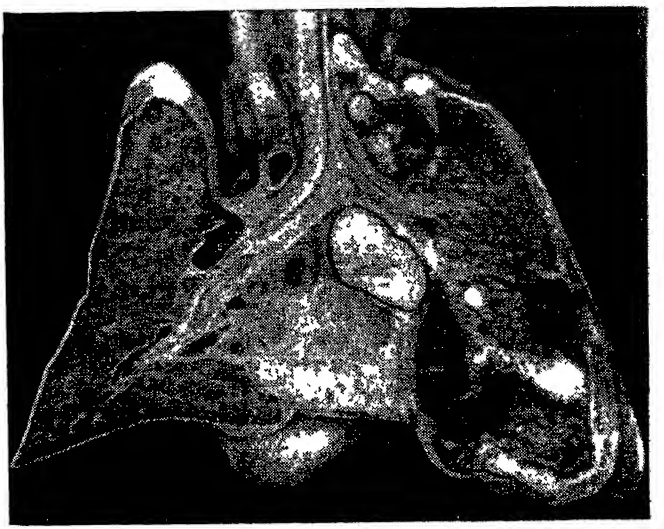


Fig. 6. Primary caseous pulmonary focus and caseous necrosis of the regional lymph nodes (after Ghon)

stage fibrinous-cellular pneumonia is observed, in whose centre a process of intensive nuclear degeneration sets in, indicating the beginning of necrosis. In such fibrinous-cellular alveolitis, the cells observed in the exudate are apparently alveolar macrophages. Leucocytes have not been noted at this stage. Subsequently, a circular caseous-pneumonic focus develops accompanied with fibrinous perifocal inflammation. An area of non-specific granulation tissue forms about the periphery. Mostly, a growth of epithelioid cells is observed around the caseous pneumonic focus. The following stages include the walling-off of the lesions, fibrotic incapsulation, and the depositing of calcium and phosphorus salts in the area of caseous necrosis; occasionally even ossification occurs. In the regional lymph nodes there also develops an inflammatory exudate with subsequent caseous necrosis or, in benign cases, with the formation of a hyaline capsule and calcification (Fig. 7). Such extensive caseous necrosis of the lymph nodes is especially characteristic of the primary stage of the disease. In most cases, the primary focus is thus walled off, becomes inactive, and heals, forming a so-called solid primary complex.

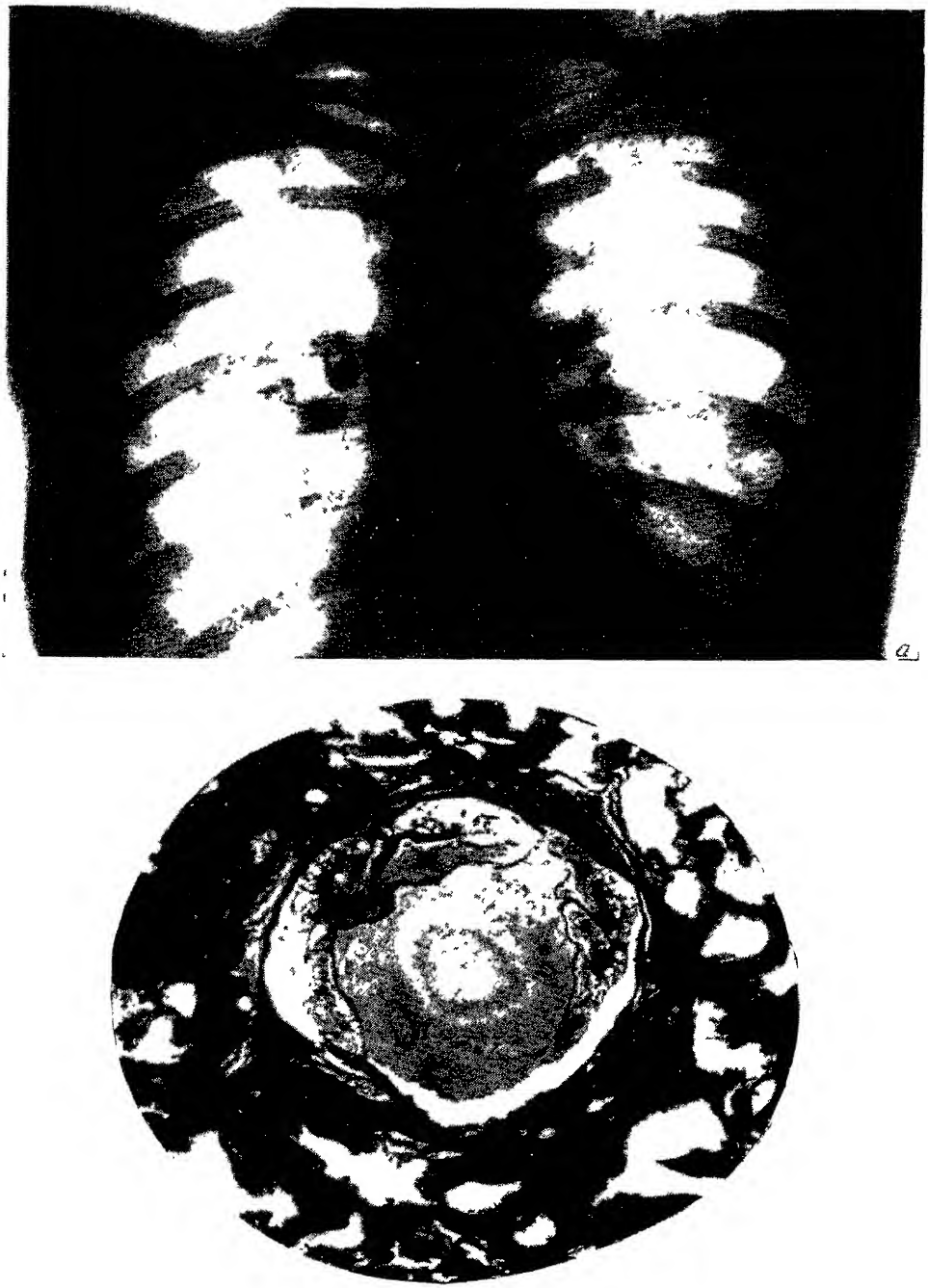


Fig 7. a—Ghon focus (radiogram), *b*—calcified and incapsulated Ghon focus with central necrosis (section after Kristeller).

Fig. 8. Acute miliary pulmonary tuberculosis with caseous necrosis of the intrathoracic lympth nodes

ROUTES OF DISSEMINATION

It should be noted, however, that the afflicted lymph nodes often retain minimal caseous changes and specific tuberculous tissue with virulent tubercle bacilli, which is particularly true of childhood. Progression of the primary complex may take place in different ways. Cases are known when the tuberculous lymph nodes adjoining the walls of a bronchus involve the latter in the process and destroy it, causing the formation of fistulae. In such broncho-fistulous forms, caseous particles containing multitudinous tubercle bacilli penetrate and are aspired into the bronchial tract, which is often accompanied by severe tuberculous pneumonia.

This, however, is neither the principal, nor, moreover, the only route of dissemination in primary tuberculosis. The lungs are provided with an extensive system of vessels and capillaries, through which the infective matter may easily penetrate from the lymph nodes into the thoracic duct, then further into the venous sinus and right heart, and thence through the wide pulmonary capillaries into the larger circuit. In this way the bacilli may be disseminated throughout the body and become lodged in various, even vital, organs. Russian workers (A. I. Kudryavtseva, Z. A. Lebedeva, V. I. Puzik) have demonstrated that dissemination of the tuberculous infection may take place at the earliest stage, even before a pronounced primary complex has developed in the affected organ.

The primary focus may develop through contact, the process spreading along the lymphatic vessels and bronchi. New areas adjoining the primary focus may become the site of exudative inflammation with subsequent caseous necrosis. The process may involve an entire lobe with the development of liquefaction and cavitation, which leads to severe intoxication and wasting. Thus, the syndrome of primary pulmonary phthisis develops (G. R. Rubinstein). Nowadays, however, such occurrences are comparatively rare. More commonly, as noted earlier, the process develops on the pattern of hemogenous and lymphogenous generalisation with the involvement of the intrathoracic and occasionally mesenteric and peripheral lymphatic system and lymph nodes. Understandably, with lower levels of resistance and an acutely proceeding primary complex, the routes of dissemination may be complex, i.e., lymphogenous, hematogenous and bronchogenic at once.

PRIMARY COMPLEX IN THE INTESTINE

As stated earlier, primary infection may likewise take place intestinally, viz., at the ingestion of infected food. In this case the primary lesion arises in the intestine proper, the process involving the regional mesenteric lymph nodes. An especially vivid example of the latter was the Lübeck disaster (Germany) when 251 infants were subjected to preventive vaccination, the vaccine proving to be "contaminated"

with virulent bacilli of human tuberculosis. As a result of this "vaccination" the children developed severe primary tuberculosis of the intestine and lymph nodes, some of these cases being revealed at autopsy. Out of the 72 children subjected to autopsy, 71 revealed a primary lesion in the intestine and the mesenteric lymph nodes.

Under normal conditions of infection, however, the primary lesion develops in the lungs and the intrathoracic lymph nodes. Russian workers (V. T. Shwaizar et al.) proved that primary tuberculosis may develop as a chronic disease whose symptoms, apart from the organic lesion proper, include caseous necrosis of the lymph nodes.

Cases are likewise on record of incomplete primary complexes where the pulmonary focus was not manifest. Finally, there are reports that occasionally a completely healed primary complex may be followed by a secondary complex with similar clinical features (true superinfection).

HEMATOGENOUS TUBERCULOSIS

Hematogenous dissemination of tubercle bacilli occurs both in the primary and secondary stages of infection. Bacillemia forms a premise for such dissemination and the emergence of hematogenous bacterial metastases. Bacillemia may originate from any tuberculous foci existing in the given organism, tuberculous lesions of the intrathoracic lymph nodes, pulmonary foci, urogenital lesions, orchiepididymitis and salpingitis being especially important in this regard.

Most frequently, the source of dissemination lies in foci with caseous necrosis. In this case the tubercle bacilli are washed out with the blood stream and lodged in the tissues. An essential factor here is the level of body reaction and the sensitivity of the organs and tissues as well as their susceptibility to bacterial metastases.

Hematogenous tuberculosis may be observed either as foci of productive inflammation, or as a tubercular eruption, or, lastly, as miliary necrosis, the lungs displaying a picture of miliary bronchopneumonia (Fig. 8).

A. I. Strukov distinguishes three basic types of hematogenous tuberculosis: (1) generalised; (2) chiefly pulmonary, and (3) chiefly extrapulmonary.

The *first* type includes acute miliary tuberculosis, occasionally assuming the form of *sepsis tuberculosa acutissima,* and in a number of cases complicated by tuberculous meningitis.

Certain subacute forms of hematogenous dissemination and the rare cases of chronic miliary tuberculosis should also be referred to the generalised hematogenous type.

The *second* type with predominantly pulmonary localisation includes the different varieties of chronic hematogenous tuberculosis (Fig. 9). These include both the limited (hematogenous apical eruptions) and the more generalised cases with large or small foci. In the primary period, when the pneumoparenchyma has not yet been

Fig. 9. Chronic pulmonary tuberculosis with hematogenous dissemination

devascularised and there is no marked sclerosis, the foci easily resolve under the effects of modern chemotherapy. In malign cases, the process may be aggravated by superimposed infiltration. In a number of cases thin-walled cavities are formed, the process spreading further bronchogenically.

As regards the *third* type of hematogenous dissemination with a preponderance of extrapulmonary metastases, the tubercle bacilli circulating in the blood are deposited in different organs, the development of lesions in which determines the clinical picture of the disease. To this group we refer hematogenous metastases in any organs, especially the urogenital and skeletal systems, skin, eyes, etc.

In chronic hematogenous tuberculosis of the lungs, concomitant emphysematous changes and pleural involvement should be taken into account. Very often the first symptom of hematogenous dissemination in the lungs is pleurisy with effusion. About 10 per cent of patients with open forms of tuberculosis earlier had pleurisy with effusion. Polyserositis, in particular, tuberculous lesions of the peritoneum—tuberculous peritonitis—occurs either as the immediate result of bacterial dissemination or as a concomitant of tuberculous mesenteritis.

Special note should be made of the extremely sluggish chronic forms of hematogenous pulmonary tuberculosis accompanied by sclerosis and emphysema which gradually lead to overloading of the right heart.

SECONDARY TUBERCULOSIS

Secondary tuberculosis includes all forms of the disease which arise after the healing of the primary complex. Usually, the process develops after varying intervals as a result of reinfection. In its present-day meaning, the term reinfection denotes the development of the disease as a result of repeated endogenous or exogenous invasion.

In the early 20th century, when it was assumed that pulmonary phthisis developed from apical foci, disseminating craniocaudally and involving successive new sections of the lungs, such apical foci were thought to be the result of aerogenous infection. But with the emergence of new evidence, in particular that *Myco. tuberculosis,* invading the body in primary infection, may remain dormant in the organs, especially in the lymph nodes, for more or less considerable lengths of time, retaining its pathogenicity—new interpretations were advanced. It became evident that under the effects of unfavourable factors reducing body resistance, the resident tubercle bacilli may produce lymphogenous or hematogenous metastases. In particular, apical foci may likewise be the result of hematogenous dissemination (Fig. 10). Such endogenous reinfection may spring from any clinically quiescent or even calcified foci. Thus, according to A. I. Strukov, calcified foci were the cause of exacerbation and relapse in 12 per cent of all cases. On such occasions the disease may spread bron-

Fig. 10. Foci of hematogenous seeding (Simon's foci) in pulmonary apex at primary tuberculous complex

chogenically, e.g., when, owing to liquefaction of a quiescent focus, the caseous particles with *Mycobacterium tuberculosis* are aspired into the adjoining parts of the lung.

Thus, both endogenous and exogenous reinfection may take place.

At present, it is still somewhat difficult to state whether reinfection in each given case was endogenous or exogenous. There is reason to believe, however, that a great number of newly observed foci are the result of endogenous reinfection. It must be noted that any rein-

fection focus, whatever its origin—endogenous or exogenous—develops against a background of changes in body reaction caused by the primary tuberculous infection. In other words, secondary lesions emerge and develop as a result of reduced resistance on the part of the allergic organism. The evolution of such foci is marked, chiefly, by an exudative-inflammatory type of reaction with hyperergy, or else a short spell of exudative inflammation is followed by predominantly productive development with less pronounced hypersensitation.

Focal (Nodular) Tuberculosis

According to A. I. Strukov, the initial morphological manifestation of secondary tuberculosis is focal tuberculosis.

The changes begin in the apical segments, most commonly in the right lung. Tuberculous granulation tissue and tubercles undergoing caseous necrosis emerge in the minor bronchi and bronchioli. Caseous endobronchitis develops, involving the pneumoparenchyma, i.e., the alveolar ducts and alveoles. In this way, the foci of tuberculous bronchopneumonia, described by A. I. Abrikosov in 1903, develop within an acinus or segment. These foci mostly tend to become incapsulated and calcified. Occasionally, however, the development of connective tissue around the lesion leads to the emergence of fibrotic foci. These unhealed yet frequently inert foci contain the pathogen in a latent state, liable, however, on reduction of body resistance, to cause further progression.

Manifest progression of the arising changes usually proceeds with a preponderance of exudative inflammation. But the course of the disease, as stated earlier, depends on body resistance, i.e., the level of allergy, natural resistance and specific immunity.

Clinically, two types of progression are observed, namely, benign and malign. This does not mean, however, that the development of lesions in the former invariably tends towards involution, or that the latter is predominantly evolutive. In every instance there are alternating phases which cannot be pictured too simply. Thus, in some cases with a benign course, the pneumonic attack is arrested by therapy, the inflammatory exudate undergoes resorption and the residual caseous foci are incapsulated. Conversely, in malign cases, the caseous necrosis resorbs, forming a cavity, and new bronchogenic foci (metastases) arise after more or less prolonged remission. But not infrequently the course is marked by the alternation of acute stages and quiescence, attacks and remissions, and is conditional on the level of body resistance, allergy and immunity.

Infiltrative-Pneumonic Forms, Exudative Tissue Reaction

As mentioned earlier, progression proceeds with a preponderance of exudative inflammation. The invasion of the lower airways by tubercle bacilli is followed by the development of a specific macro-

Fig. 11 Caseous pneumonia

phage reaction. The cells of the alveolar epithelium undergo metaplasia, and the bacilli are phagocytised. But, occasionally, they reproduce intensively in the lung, which presents a highly fertile medium for the growth of *Myco. tuberculosis*–an obligate aerobe.

In such circumstances, the development of exudative inflammation is accompanied by exudative alveolitis with the emergence of macrophages, fibrin and a small number of polynuclears.

Three types of exudative inflammation may be distinguished: (1) fibrino-macrophagous; (2) fibrinous, and (3) exudative with a preponderance of polynuclears.

With the development of infiltrative pneumonic changes in the lung, a varying part of the exudate undergoes caseous necrosis. In the process, the fibrin loses its fibrillary texture, thickens and becomes homogenous. The cells of the alveolar membrane and the polynuclears also lose their structure. The elastic fibres are the only elements offering more or less prolonged resistance to the progressive necrosis.

With an unfavourable course, the caseously degenerated mass softens, absorbing water and liquefying as in pyogenic processes. This partly takes place under the influence of proteolytic ferments and leucocytes. Apart from liquefaction, the massive caseous areas occasionally undergo sequestration (Fig. 11). The emerging degenerative cavities contain enormous multitudes of tubercle bacilli.

With a more favourable course, the caseous focus is observed to undergo dehydration, walling-off and incapsulation. More often, however, extensive caseous necrotic foci are seen to undergo liquefaction.

Fig. 12. Tuberculoma in resected lung segment

Only in the last decade, with the use of modern chemotherapy, caseous necrotic lesions have been observed to undergo walling-off and incapsulation with the formation of so-called tuberculomata (Fig. 12).

Productive Tissue Reaction

Productive tuberculous inflammation (Fig. 13), the most vivid example of which are tubercles, does not occur independently but is accompanied by exudative changes. Occasionally, however, productive inflammation may predominate, which takes place at higher levels of resistance. Usually, tubercle formation is followed by a growth of connective tissue.

Productive inflammation often occurs in chronic cases, although at times, as, for example, in acute miliary tuberculosis, typical tubercles may be observed. On such occassions we speak of malignant proliferation. But the spread of tubercles, e.g., in the lungs, is likewise observed in chronic hematogenous cases in the form of what is known as "cold" dissemination.

W. Hueck picturesquely compares the emergence of an inflammatory focus with the concentric waves spreading around a stone dropped into water. Under the immediate toxic effects of the bacilli on the

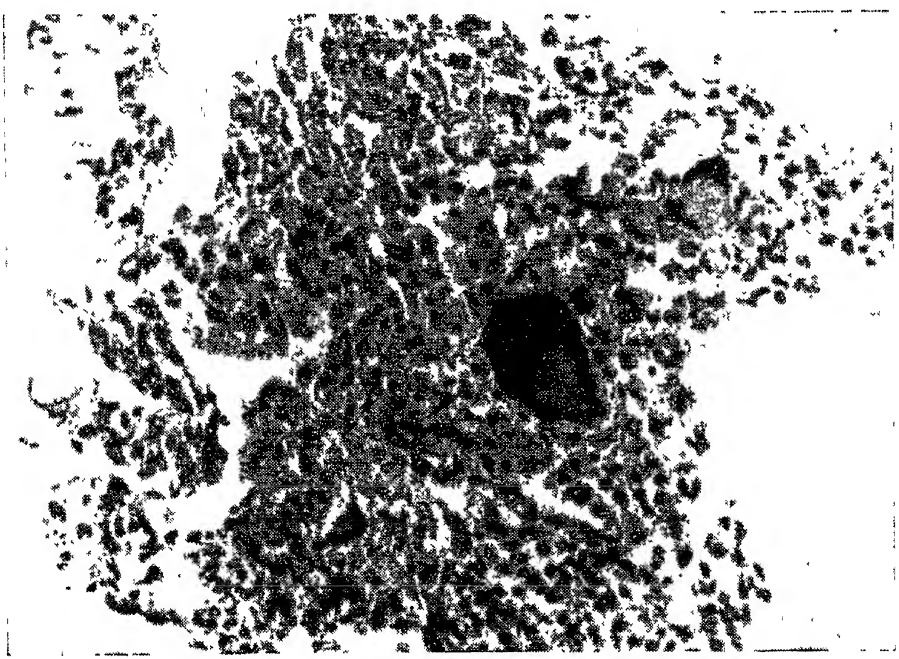


Fig. 13 Productive tuberculosis; tubercle with giant cells

tissues, a necrotic nucleus appears in the focal centre on the edges of which an area with obstructed circulation develops in the form of an exudate, which is later surrounded by granulation tissue—the result of cellular proliferation.

The microscopic structure of a tubercle is pictured as follows. The necrotic centre is surrounded by a palisade of epithelioid cells, in their own turn encompassed by lymphocytes which appear as circular cells. Under the effects of toxic agencies some of the cells undergo incomplete fission, the nuclei dividing and the protoplasm remaining intact, and giant cells of the Langhans type emerge. The nuclei are distributed about the periphery, tubercle bacilli often being seen in the centre, causing gradual necrosis of the cells. The foci of exudative inflammation and the conglomerates of tubercles may undergo more or less massive necrosis, or else, with adequate resistance, resorption or fibrous transformation may take place. Exudative inflammation, however, is more often accompanied by massive necrosis—a manifestation of hyperergy.

Cavitation and Progression

The development of a cavity in a lung, lymph node or the kidneys heralds the onset of a new, destructive stage in the disease, particularly as regards the lungs and kidneys. It is scarcely surprising therefore, that cavitation is sometimes called a "second disease".

Cavities may appear during both the primary and secondary periods of infection. Pathogenetically, according to T. N. Oleneva, the following types of cavitation are distinguishable:

1. Alterative or (according to V. G. Shtefko) perifocal, arising at the site of a former focus;
2. Pneumoniogenous, developing from an infiltration and a pneumonic focus;
3. Bronchogenic, developing from altered bronchi (bronchiectatic cavitation).

In the course of time, the walls of a cavity undergo a process of organisation, giving rise to pictures of so-called fibrocavernous tuberculosis (Figs. 14 and 15). Here, instead of incapsulation, symptoms of progressive degeneration may be observed.

Histologically, depending on its genesis, the cavital structure may demonstrate certain distinctions. As the cavity develops, it shows:

1. An internal necrotic layer;
2. An intermediary layer situated between the capsule and the necrotic stratum, with distended capillaries, whose rupture occasionally serves as the cause of hemoptysis (the changes occurring in this layer for a long time retain a non-specific character);
3. A capsule of varying thickness depending on the age of the cavity, which develops at the expense of non-specific elements, such as macrophages, fibroblasts and capillaries. The collagenous fibres thicken and combine with the other elements to form a sizeable capsule.

Fig. 14. Fibrocavernous pulmonary tuberculosis (section after Kristeller)

Fig. 15. Cavity in superior lobe of left lung at fibrocavernous pulmonary tuberculosis

In the case of organised cavities, the capsule is often surrounded by pericavernous atelectasis which is of special importance since at closure the re-expanding atelectatic area plays the part of reserve parenchyma. A special kind of structure is observed in the so-called stamped cavities which occur in hematogenous dissemination (see below). These cavities have thin walls and usually contain a comparatively small amount of exudate.

As stated earlier, the incidence of a cavity with walls and content abounding in *Myco. tuberculosis,* is fraught with the grave danger of bronchogenic dissemination. Hence, alongside general measures to strengthen resistance, special steps should be taken to promote the closure and healing of the cavity. Today this can be done more frequently than previously thanks to the use of chemotherapeutic drugs, collapse therapy and various surgery.

Mechanism of Cavity Closure and Healing

The best form of healing is by cicatrization (Fig. 16), the next best comprising the development of a focus in which the caseous mass becomes desiccated and incapsulated (Fig. 17). Healing is preceded by closure, or else the cavity is filled with lymph. Lastly, particularly today, with the increasing use of continuous chemotherapy, cases are observed when the healing process involves not the cavity proper, but its walls. This is followed by the development of a so-called bullous or cystose cavity with thin walls and without the internal necrotic layer. In such cases, the healed cavity is replaced by a cyst, which, however, is comparatively seldom met (TN. Oleneva) (Fig. 18).

Fig. 16. Healing of cavity by cicatrization

Fig. 17. Healing of cavity by incapsulation

Fig. 18. Healing of cavity wall by encystment

The mechanism of closure and healing requires additional research. Coryllos pointed out the considerable importance of occlusion of the draining bronchus. Moreover, as he believes, the closure (obliteration) of the lumen of such a bronchus is a prerequisite for healing. Bronchial occlusion is followed by aspiration of air from the cavity and, subsequently, by the latter's closure. Besides, the resultant absence of ventilation in the cavity gives rise to a shortage of oxygen which is fatal for such an obligate aerobe as *Myco.tuberculosis.* Conversely, occlusion of the draining bronchus may presumably in some cases hinder sloughing and thus stimulate progression.

In any case, closure and healing are usually linked with increased general resistance and desensitation. Fresh elastic cavities are more prone to reparative changes. The healing and closure of an organised cavity is mechanically handicapped by the rigidity of the cavity walls.

Tuberculosis of the Oral Cavity and Upper Respiratory Tract

Oral tuberculosis is extremely rare, although in exceptional cases there may be a primary lesion of the tonsils.

As regards ulcerous lesions of the oral mucosa and tongue, these are mostly concomitant with pulmonary tuberculosis, being accompanied by severe pain which impairs nutrition.

Laryngeal tuberculosis usually assumes the form of productive lesions and ulcerous-exudative changes. Hematogenous eruptions are likewise observed. Depending on the course, the inflammatory changes tend either to resorb and heal, leaving scars, or caseous foci develop with subsequent ulceration. Laryngeal tuberculosis is sometimes complicated by perichondritis.

Fig. 19. Epithelisation of larynx after streptomycin treatment of ulcerous tuberculosis. Tuberculous granulations with giant cells in laryngeal submucosa

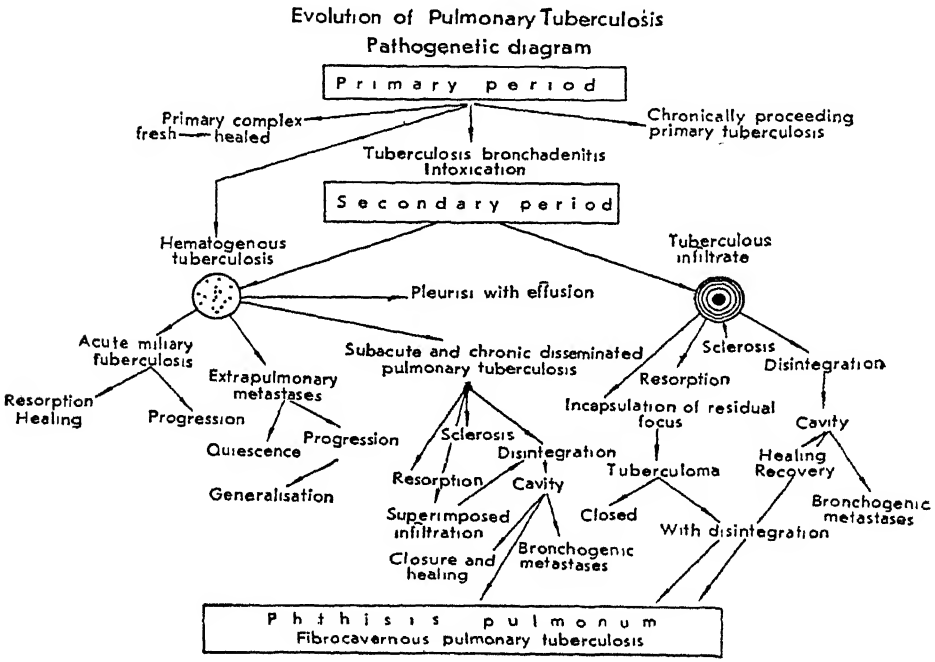
The process usually affects the vocal cords, posterior wall and epyglottis. This recently severe disease, which was often accompanied by agonising dysphagia, is readily amenable to streptomycin and phthivazid. The inflammatory lesions are partly resorbed and partly cicatrized and epithelised (Fig. 19).

Bronchial Tuberculosis

Primary lesions of the bronchi are a rare occurrence. Usually, they are associated with marked changes in the lungs, but selective lesions of the trachea and bronchi may occur as well (see below). The disease may give various pictures—from sparse tubercles to caseous infiltrations and caseous endobronchitis leading to ulceration and destructive processes. Later, fibrous stenoses and bronchiectases may develop at the site of the lesion. In addition, specific perifocal bronchiolites and brochites may also be observed.

F. Schwartz attributes a special role in the development of pulmonary tuberculosis to broncho-fistulous changes which he observed in the form of fresh bronchial lesions or scars in 25 per cent of all cases on general sectional material and in up to 90 per cent on autopsies of lethal cases of tuberculosis. In a radiological, histotopographic, and histological study conducted by I. P. Solovyova on 104 cases of pulmonary tuberculosis, broncho-perforative changes were found in 28 of them, i.e., in 26.5 per cent. K. A. Deli mostly found such changes in primary tuberculosis.

The following diagram, which deals with both primary and post-primary stages of the disease, shows the relationship between various forms of pulmonary tuberculosis, representing, in effect, the successive links of a single pathogenetic chain.



The diagram outlines the ways in which tuberculosis may develop and the potentialities of involution and healing inherent in different stages of the disease. It should be noted that in hematogenous dissemination progression may develop not only via the blood, but through infiltration superimposed on the hematogenous changes. As evident from the diagram, degeneration and cavitation may occur both in hematogenous and infiltrative forms, and *phthisis pulmonum* may be the culmination of various forms of pulmonary tuberculosis. With prompt therapy, however, reparative processes may prevail at any stage, all depending on the particular patient's general resistance level.

As has been stated above, tuberculosis not only entails local changes, but develops as a general infectious disease. The picture may likewise include extensive dissemination in the form of early generalisation directly following the primary stage or, at later dates, may assume the form of hematogenous metastasis.

Tuberculous foci may arise in any organ. In chronic cases such extrapulmonary lesions may be clinically predominant, the picture assuming additional features connected with the functional role of the afflicted organ or system.

Tuberculous lesions of the viscera and serous membranes are of special importance. Lesions of the latter (pleuritis, pericarditis, peritonitis) are never primary, but are usually concomitant with the basic process developing in the organs. Thus pleurisy may often accompany tuberculous lesions of the lungs or the mediastinal lymphatics. Tuberculosis of the intrathoracic lymph nodes may likewise be the source of pericarditis. Tuberculosis of the intestine and the mesenteric lymph nodes may give rise to tuberculous lesions of the peritoneum in the form of exudative or plastic peritonitis.

Tuberculosis of the Alimentary Tract

Tuberculosis of the stomach is an extreme rarity. Until recently intestinal tuberculosis occurred as a severe complication in open forms of pulmonary tuberculosis. Over the last ten years, thanks to chemotherapy, it has become considerably less common. According to our own sectional findings, in 1947, 57.6 per cent of cases of tuberculosis were intestinal and in 1957, only 11.9 per cent. In more than 70 per cent of all cases the disease is amenable to treatment.

Intestinal tuberculosis may result from the ingestion of sputum containing *Mycobacterium tuberculosis*. In addition, the possibility of hematogenous invasion (D. A. Manucharyan et al.) must also be considered. The lesion is mostly localised in the intestinal wall, in areas containing lymphatic tissue (Peyer's patches, solitary follicles). The developing infiltrations mostly ulcerate, forming so-called round lenticular ulcers with undermined edges. The lesion may proliferate to the serous membrane, involving the peritoneum. Ulceration mostly develops during exudative inflammation. Productive tuberculosis is accompanied by thickening of the intestinal wall and stenosal changes.

A vivid example of this type of process is hypertrophic ileocecal tuberculosis.

Urogenital Tuberculosis

Urogenital tuberculosis develops as a result of hematogenous generalisation.

In childhood hematogenous generalisation mostly results in lesions of the bones and joints, lymphatic system and middle ear, whereas

after the age of 20, tuberculosis may affect the lungs, intestine and larynx as well as the urogenital system. It must be emphasised that in urogenital tuberculosis the primary lesion is mostly localised in the kidney, while later the disease assumes all the features of a systemic affliction. Here, too, the process spreads with the flow of urine, which was confirmed by Wildbolz who observed combined urogenital tuberculosis in 70 per cent of afflicted males and only in 5 per cent of females.

Renal tuberculosis is mostly unilateral, assuming a chronic course. Usually, the disease begins at working age. In children such lesions are considerably less frequent. Renal tuberculosis shows a marked tendency towards healing.

At reduction of the general and local resistance, the microscopic focus erodes into the urinal ductule. An ulcerous lesion forms about the papilla with the subsequent development of caseous-cavernous renal tuberculosis marked by persistent discharge of *Mycobacterium tuberculosis* with the urine (Fig. 20). Lesions of the bladder are usually

Fig. 20. Destroyed kidney with tuberculous cavities

post-primary, arising through extension from the kidneys and exhibiting minimal foci in the mucosa, either with or without ulceration.

Lesions of the prostate and seminal vesicles may develop hematogenously. Mostly, however, prostatic lesions are associated either with renal tuberculosis or tuberculous epididymitis.

Tuberculous epididymitis frequently represents the primary lesion in urogenital tuberculosis.

The female genitals are usually affected hematogenously. In 80 per cent of cases the process is localised in the tubes. In tuberculous adnexitis, concomitant peritoneal lesions are observed in 60 per cent of cases. The latter may be accompanied by lesions of the ovary (tuberculous abscesses).

Tuberculous lesions of the tubes may give rise to a pyogenic process (*pyosalpinx tuberculosa*).

PATHOGENESIS AND PATHOLOGICAL ANATOMY OF BONE-AND-JOINT TUBERCULOSIS

Tuberculosis of the bones and joints is mostly observed in childhood as part of the primary complex, being the result of hematogenous metastasis and occurring more frequently in boys than in girls, in the ratio of 6 to 4 (Johannson). As commonly known, the disease mostly involves the vertebrate bodies and minor bones with richly vascularised *substantia spongiosa.* In tubular bones the infection usually affects the epiphysis.

The most essential feature of bone tuberculosis is internal ostitis which is characterised not so much by lesions of the bone proper, but by the development of peculiar and specific pictures of osteomyelitis.

The lesion may take two forms: (1) granulation-type and (2) caseous osteomyelitis.

PREDOMINANTLY GRANULATION-TYPE BONE TUBERCULOSIS

Foci of a greyish or greyish-red colour appear in the bone marrow, surrounded by a growth of granulation tissue. The tuberculous process in the bones, especially at onset, assumes a productive, proliferative (T. P. Krasnobayev) and focal character. Diffuse tubercles in the marrow are observed only in acute miliary tuberculosis.

Such a focus of chronic inflammation in the marrow causes lacunar destruction of the surrounding bone tissue. In benign cases this is followed by incapsulation or fibrous transformation of the focus, and in a number of cases by osteal neoplasm. Occasionally, the barrier of connective tissue may break down, the process continuing its development. As a result of caseous necrosis a cavity may form in the bone tissue which may erode into the adjacent joint.

Occasionally, destruction takes place without suppuration, assuming the form of *caries sicca.*

CASEOUS-NECROTIC BONE TUBERCULOSIS

This type of infection is accompanied by extensive destruction of the tissues. Caseous necrosis affects both the marrow and the bone tissue proper. Subsequently, as a result of autolysis, the caseous masses are liquefied with the accumulation of creamy sand-like pus (bone sand) having a low content of tubercle bacilli. The purulent focus may erode into a joint or spread subperiosteally. Erosion of the periosteum is followed by the development of the clinically-common cold abscess.

Fig. 21. Tuberculosis of the spine. Hump (*gibbus*)

Special note must be made of spinal lesions involving the thoracic and lumbar sections, associated with the compression resulting from destruction of the vertebrae. The lack of adequate treatment may lead to the development of gross spinal deformities and humps (*gibbus)* (Fig. 21).

TUBERCULOSIS OF THE JOINTS

Usually, joint involvement follows the erosion into the joint cavity of a subchondral tuberculous focus localised in the epiphysis.

On extremely rare occasions, the synovial membrane is affected hematogenously.

In tuberculosis of the joint tissues, tubercles in the synovial membrane are accompanied by reactive inflammation.

The following forms of joint lesions are distinguishable: (1) *Hydrops tuberculosus;* (2) *Fungus tuberculosus;* (3) *Caries sicca;* (4) Tuberculous panarthritis.

In the first form (*hydrops*), serous or serofibrinous exudate accumulates in the joint. In cases of *fungus tuberculosus* there is a considerable development of specific tuberculous granulation tissue issuing from the synovial membrane. In cases when the process assumes the form of *caries sicca* the granulation tissue is less evident and tends to retract. Caseous-purulent lesions of the joints are a result either of rapid liquefaction of granulation tissue or erosion of a bone abscess into the joint.

Tuberculosis of the Skin

Tuberculous lesions of the skin are markedly polymorphous. These lesions are seldom the outcome of exogenous infection. Mostly, as in other extrapulmonary localisations, they develop hematogenously. Occasionally, the process originates from tuberculous lymph nodes (*scrofuloderma*). Women and children are more often affected than men.

The most common form of skin tuberculosis is *lupus vulgaris*, a process based on productive inflammation. The disease assumes the form of characteristic nodules which present light- or dark-yellow hyperemic girdles. The disease mostly affects the face. The nodules have a distinctly characteristic appearance when a microscopic slide is pressed to the skin and are vividly seen on the bloodless background.

The disease is known to take different forms, viz., *lupus hypertrophicus, verrucosus, squamosus, exulcerans, serpiginosus.* A special form of the disease is the previously mentioned *scrofuloderma, tuberculosis colliquativa cutis*, an outcome of extension mostly from the underlying lymph nodes or joint, especially in fistulous forms.

Tuberculosis of the Eye

One of the common manifestations of tuberculous allergy is phlyctenular conjunctivitis—a frequent concomitant of primary tuberculosis.

Tuberculosis of the eye occurs in the form of cerato-conjunctivitis, iritis, choroiditis, uveitis and retinitis. Combined localisations are observed as well. Usually, the eye lesion is the result of hematogenous dissemination, seldom occurring in chronic forms of pulmonary tuberculosis.

Tuberculous iridocyclitis starts with the appearance of tubercles (stage I). Subsequently, widespread exudative iritis is observed with acute toxic manifestations (stage II). These symptoms are mostly witnessed in adolescence. Tuberculous uveitis is regarded as the third stage of the disease.

Tuberculosis of the Central Nervous System
Meningitis Tuberculosa

This localisation is usually the outcome of hematogenous generalisation which may occur in both primary and post-primary periods. The source of bacterial dissemination here is a caseous focus, e.g., in a lymph node or in the region of the genitals, as in tuberculous epididymitis or testitis. The condition may also develop into general miliary tuberculosis with one of its localisations in the central nervous system, particularly the meninges. There are likewise cases of hematogenous bacterial metastasis limited to the central nervous system when the clinical picture is dominated by a lesion of the latter.

Tuberculous lesions of the meninges in the form of tuberculous leptomeningitis are the most important in practice. In 75 per cent of all cases tuberculous meningitis is accompanied by acute miliary tuberculosis.

It must be emphasised that tuberculous meningitis very often develops in the primary period, whence it is most frequent in childhood. As Kment has correctly noted, basilar leptomeningitis does not result immediately from hematogenous infection of the meninges, but emerges at primary mycobacterial invasion of the choroid plexus from which the disease extends to the meninges. Such a view may also serve to explain the basal localisation of the lesion.

These conjectures, however, have not been fully confirmed. Apparently, essential importance should be attributed to the emergence of conditions under which the mycobacteria, on surmounting the hematoencephalic barrier, penetrate into the spinal fluid and spinal cavity. This occurs, apparently, at critical hypersensitation. In this case the bacteria meet with reactive mesenchyma in the *telae chorioideae*, causing a lesion of the basal segments.

The onset of meningeal tuberculosis is marked by pronounced exudative inflammation due to the invasion of the spinal fluid by mycobacteria. In typical cases there is a jelly-like exudate localised between the *pons* and *chiasma nn. opticum*, reaching the pituitary and the silvian fissure. The vascular picture at this stage is obscure. The cerebral tissue is edematous and hyperemic. The *dura mater* is also involved in the process. Further progression is likewise dominated by exudative and caseous changes, the emergence of tubercles being considerably less frequent. In certain cases, however, such eruptions may be observed in the meninges, but do not necessarily involve the penetration of the infection into the spinal fluid. In some cases, when the latter does not occur, the tubercle conglomerate begins to form without preliminary exudation.

As mentioned earlier, a major factor in the development of tuberculous meningitis is general body reaction coupled with drastic hypersensitation to tuberculosis. In some cases the process involves the cerebral tissue (meningo-encephalitis).

CHAPTER III

ANAMNESIS AND SEMIOLOGY

One of the main features of tuberculosis is the variety of forms it can take. This follows, primarily, from the nature of the infection proper and the accompanying intoxication on the one hand, and the multiformity of changes occurring in the organs and systems and impairing their functions on the other. Such changes depend in their development on general body reaction and resistance.

ORIGIN OF SYMPTOMS

Principally, the symptoms and functional disturbances occurring in tuberculosis are determined by the following:

1. The initial state of the body and its resistance;
2. The nature of the lesion, i.e., the focus, in the broader sense of the word;
3. The degree of intoxication.

It is essential to note the close correlation between the body reaction and the behaviour, as it were, of the focus. Apart from pronounced manifestations, there are frequent occasions when the disease, especially at onset, assumes a latent, almost symptomless course. There have been cases of unnoticed tuberculosis (*tuberculosis inapercepta*). Therefore, in examining a case, careful establishment of anamnesis is particularly important. Anamnestic study and assessment of factual material related to previous illnesses, particularly if certified by a physician (anagnosis), are a vital premise for prompt diagnosis of tuberculosis.

CHILDHOOD TUBERCULOSIS

An essential feature of childhood tuberculosis is that, pending invasion and tuberculin conversion, the organic changes may not yet be apparent whereas intoxication may already be evident, testifying to concealed changes. After the development of a primary complex, when the pulmonary process is already arrested (Ghon's hard tubercle), there may still be active tuberculous lesions in the lymph nodes of the thoracic and, sometimes, the abdominal cavities. In such cases

the disease appears in the form of tuberculous intoxication of varying degrees accompanied by disturbances of the vegetative functions, anorexia, and occasionally insomnia. The appropriate situation has been excellently described by A. A. Kissel. In such conditions, irregular subfebrile temperature with an increase of basic metabolism and sweating frequently occurs. A tendency to chills and repeated bronchial catarrh is noticeable, associated with allergy and concomitant hypersensitiveness to meteorological effects. As mentioned earlier, moderate functional disturbances may accompany early intoxication.

ONSET AND COURSE IN ADULTS

Adults usually give a clearer picture, mostly related to the post-primary period, pulmonary lesion being witnessed in 85 to 90 per cent of cases. In 60 per cent we have observed an acute onset often masked as influenza (so-called pseudo-influenza). An acute, normally short-term, febrile period (1-2 weeks) either terminates in a remission, or else slight subfebrile temperature fluctuations persist, occurring mostly in the evening and occasionally in the morning (*typus inversus*). In the former case, the patient often ignores the influenza, and only a fresh exacerbation takes him to the doctor if adequate dispensary follow-up has not been begun. It should be remembered that primary tuberculosis usually proceeds as a series of attacks and remissions. In benign cases, quiescence culminates in recovery, but in others relapses are observed.

Repeated exacerbation, relapses and their outcome are dependent on individual resistance and the promptness and adequacy of treatment, primarily chemotherapy As noted earlier, an acute attack is usually connected with an inflammatory process in the lungs, and far less often in other organs.

ANAMNESIS

Careful establishment of anamnestic data is vital for early detection of the disease. First of all, there should be complete information on tuberculous cases in the family, especially with positive sputum, minding that morbidity among contacts is three to four times higher than among the general population.

It is important to delineate the patient's development, noting the illnesses suffered in childhood (measles, whooping-cough, bronchitis, pneumonia), and to ascertain whether BCG vaccination was instituted. Occupational hazards (dust, noxious gases, radiation) should be recorded with past instances of abnormal temperature, night sweat and functional disorders, e.g., excessive fatigue after customary work. In women note should be taken of dismenorrhea frequently associated with tuberculous intoxication, to which the endocrine and vegetative systems are highly sensitive. Occasionally, these disturbances are concomitant with a tuberculous lesion of the genital region.

Apart from general symptoms, it is important to record instances of hemoptysis, coughing and expectoration, noting the results of sputum tests, if taken. Attention should be afforded to pains in the chest at breathing (pleuritis) or pains with dyspnea (spontaneous pneumothorax).

Special regard should be paid to diseases lowering resistance to infection such as *diabetes mellitus*, leukoses, congenital cardiac lesions or past functional disturbances in the gastrointestinal tract (hypochylia, spastic colitis), etc.

It is desirable to know the gravity of past illnesses, the frequency and duration of diseases of the upper respiratory tract, bronchi and lungs. It is essential that the type of treatment applied, the time and frequency of residence at sanatoria, and the kind, dosage, duration and effects of drug therapy be found out. A matter of special interest are side-effects after antibacterial treatment.

GENERAL SYMPTOMS

Fever. Sweat

It is well known that temperature increases and anomalies of the daily curve often accompany active (progressive) tuberculosis. In acute attacks the temperature reaches 38 or 39°C and more. In quiescence, it is subfebrile or low subfebrile (37.2 to 37.5°C). Not infrequently the initial tuberculous changes in the lungs and other organs are accompanied by irregular subfebrile temperature.

It should be remembered, however, that subfebrile temperature is not invariably associated with tuberculous infection and intoxication. It is often evidenced in chronic tonsillitis, inflammation of the auxiliary nasal cavities, inflammatory conditions of the heart and diseases of the biliary ducts, chroniosepsis, etc. Increased variations between morning and evening readings (more than 0.5°) are quite typical of temperature rises accompanying tuberculous intoxication. A characteristic symptom of tuberculosis is the lability of the temperature. In cases of distinct hypersensitation with a sharply positive tuberculin reaction, short temperature rises (from 1 to 2 hours) are observed. With an active tuberculous focus, especially in the lungs, temperature increases may be caused even by such moderate physical exertion as a half-hour walk, or emotional strain, the effect of physical stress being comparable to the reaction to tuberculin injection. At one time, subcutaneous tuberculin injections (Koch's test) were used in differential diagnosis to detect a latent focus. If such a lesion was apparent, there was a general febrile reaction, a focal response with increased expectoration and a local reaction at the site of inoculation. At present, this method is applied only in exceptional circumstances.

In contrast to certain cyclic infections, temperature during tuberculosis is atypical. Mostly there is a temperature rise in the evening

(from 4 to 7 p.m.) and much less frequently in the morning (*typus inversus*).

The course of the disease is marked by a number of peculiarities which help to diagnose various clinical forms. We may thus note:

1. Fever during acute attacks or exacerbation (lasting from 1 to 3 weeks) in both primary and post-primary stages at tuberculous infiltration or pneumonia and acute generalisation; temperature up to 39°C and more, gradually or, with chemotherapy, critically returning to lower figures;

2. Chronic febrile conditions, sometimes wave-like, with subfebrile temperature of 37.2 to 37.5°C, in forms localising in the peripheral, thoracic and abdominal lymph nodes;

3. Intermittent fever to the extent of *febris hectica* in grave pulmonary forms (*phthisis pulmonum*), at exacerbation of fibrocavernous tuberculosis or in caseous pneumonia; wide daily variations up to 2 degrees and more; profuse sweat;

4. Labile temperature, thermoregulatory disorders under mental or physical strain—temperature increases reaching several tenths of a degree;

5. In women, premenstrual temperature rises reaching several tenths of a degree, not infrequent in active tuberculosis.

The febrile syndrome is mostly accompanied by a marked rise up to 20 to 30 per cent in basic metabolism and by oxygen deficiency, as in more extensive pulmonary lesions, e.g., subacute hematogenous dissemination and pneumonic forms. Fever is often accompanied by sweating and, in severe forms, by profuse nocturnal sweating causing considerable wasting.

It is well known that tuberculous intoxication causes disturbances in the regulation of physiological functions, particularly affecting the central and vegetative nervous systems, residual symptoms occasionally persisting in convalescence.

This particularly applies to sweating, which is evident in patients whose bed hygiene is faulty, e.g., the use of overwarm bedclothes in poorly ventilated rooms.

Wasting

Wasting was regarded as a classic syndrome in progressive tuberculosis. But when it was established that a rational diet with adequate general supportive measures may prevent rapid wasting, extreme instances of it became considerably less frequent. Nevertheless, loss of weight quite frequently occurs in active forms with intoxication, being associated firstly with anorexia, especially in pulmonary cases, and secondly with metabolic disturbances in the active period, whose onset is marked by digestive trouble. Oxidation disorders are one of the main phenomena accompanying tuberculous intoxication. The vital importance of regular oxygen intake is well known, but unfor-

tunately I. P. Pavlov's definition of oxygen as a nutrient is not infrequently disregarded in practice.

To summarise, the basic symptoms of an active process are: (1) Anorexia, especially in childhood; (2) Fever; (3) Progressive wasting.

A gradual return to what is assumed to be normal weight is one of the initial signs of compensation. In recent years, with the use of chemotherapy, this occurs considerably more often than earlier.

In certain cases, inadequate diet and especially overfeeding result in anorexia, which may be caused by disturbances of glandular secretion, particularly hypochylia, which is often observed in tuberculous patients. In cases of marked and, especially, specific intestinal pathology, anorexia may occur as well.

RESPIRATORY SYMPTOMS

Pain in the Thorax

Acute piercing pain occurs in pleurisies at the outset of the disease. The sharp pain felt at inspiration or coughing hinders breathing. Abrupt pain with mounting dyspnea is often observed in spontaneous pneumothorax. Dull pain, occasionally felt in the thorax, occurs in chronic fibrocavernous processes and pulmonary cirrhoses, becoming greater in uncomfortable positions.

Sometimes, in chronic cases, there are complaints of a drilling pain in the back ("phthisic nail") perhaps indicating a lesion of the spine which calls for detailed examination (not only lung X-ray, but laterography of the spine). Frequently, pulmonary tuberculosis is accompanied by neuralgia (intercostal neuralgia) and pain in the anterior thoracic muscles (myositis). We have come across patients complaining of infrasternal pain in swallowing, with the presence of hilar tuberculosis and tuberculous bronchadenitis.

At apical lesions, the pain is focussed in the supraclavicular region.

It is worth noting that the pains mentioned are often intermittent, being associated with the weather (wind, high relative humidity, cold, cyclones), and disappear of their own accord when the weather improves.

Coughing

Coughing, whether intermittent, chronic or spasmodic, with or without expectoration, frequently accompanies pulmonary or bronchial tuberculosis, especially with a lesion in the area of the tracheal bifurcation, but is not necessarily present in all tracheal lesions. A slight cough is mostly noted in the primary forms, while attacks with profuse sputum are more often met in cavernous tuberculosis and concomitant bronchiectasis. At times the attacks are followed by vomiting due to irritation of the vagus. Dry cough is sometimes apparent in laryngeal lesions. Reflex coughing is observed in pleurisy.

It should be borne in mind, however, that at least one-third of all patients do not complain of coughs, and there is usually no coughing at primary focal changes.

Coughing, especially when of the most torturous variety or occurring in repeated fits, exhausts the patient, causing insomnia and pains in the thorax, abdominal muscles and diaphragm. Acute cough causing irritation exists in hemoptysis.

Cough control is effected by means of drugs and psychotherapy which disciplines the patient and helps him to suppress his cough by will power. Nevertheless, chemotherapy is at present the most important means of controlling coughing.

Hemoptysis

Hemoptysis is the most alarming symptom for the tuberculous patient, mostly indicating an active process. It may take the following forms:

1. Primary hemoptysis which does not affect the major vessels and is associated with allergic inflammatory processes. As is commonly known, the metabolic products of tubercle bacilli sensitise the vessels, rendering the capillaries more penetrable and paving the way for hemorrhages (hemoptysis). Hemorrhages appear as blood streaks or clots in the sputum expectorated without sharp coughing irritation.

2. Hemoptysis in destructive forms of tuberculosis with cavities and bronchiectases or, occasionally, disintegrating tuberculomata. Such cases are always more extensive, being very prone to relapse, and are accompanied by coughing with such complications as aspiratory metastases and bronchopneumonia.

3. Profuse hemoptysis, usually due to the rupture of major vessels involved in the process (Rasmussen's aneurism) (Fig. 22). Occasionally, these may cause death from acute anemia or, still more often, asphyxia, resulting from bronchial occlusion by blood clots. Yet the majority of patients overcome such complications and subsequently merely require more attention to their individual regimen. According to data obtained from the Tuberculosis Clinic of the 2nd Moscow Medical Institute, only 32 per cent of hemoptysic cases were without complications. Fourteen out of 243 cases of pulmonary hemoptysis were profuse. In 21.8 per cent hemoptysis was accompanied by aspiratory pneumonia (K. S. Aisenshtadt).

Today, when modern chemotherapy and surgery offer far greater promise of clinical recovery, the total incidence of hemoptysis is bound to decline. On the other hand, more effective treatment prolongs the life expectancy of severe fibrocavernous cases, which partly explains the somewhat higher incidence of profuse hemoptysis.

Cases are known when exacerbations were invariably followed by hemoptysis. We have repeatedly observed such occurrences, especially in hilar tuberculosis. In one such instance, in the period between 1912 and 1915, the patient suffered five gross hemoptyses between

Fig. 22. Rasmussen's aneurism. Destroyed aneurismic vessel with thrombus in cavity wall

the ages of 21 and 23 years, two of them profuse, and was restored to clinical health until 1950. That year, however, there was a relapse likewise accompanied by hemoptysis which was successfully arrested by chemotherapy, as a result of which there was no complication in the form of aspiratory pneumonia.

Initial hemoptysis is normally not a malign symptom, but mostly indicates an active process.

Complicating aspiratory bronchopneumonia after hemoptysis or pulmonary hemorrhage is usually accompanied by temperature rises; in milder cases such resorptive fever continues from 3 to 4 days, after which the temperature returns to normal or subfebrile levels.

It is correctly believed that this last circumstance indicates progressive pulmonary changes. At the advent of aspiratory pneumonia after hemoptysis, the febrile condition persists much longer, depending on the development of the process.

In two-thirds of all cases the cause of hemoptysis is pulmonary tuberculosis.

Respiratory and Circulatory Disorders in Pulmonary Tuberculosis

In primary focal forms of pulmonary tuberculosis there are no manifest impairments of a respiratory and circulatory nature apart from a certain tendency towards tachycardia (labile pulse).

The picture, however, is different in chronic forms of hematogenous dissemination, tuberculous pneumoscleroses with emphysema, pulmonary cirrhoses (retraction) with deformation of the thorax, pneumoparenchyma, bronchi and minor vessels, particularly arterioles, and mediastinal displacement towards the affected lung. In these cases there are varying degrees of pulmonary and cardiac insufficiency with mounting hypertension in the lesser circuit, i.e., the system of the pulmonary artery, gradual overloading of the right heart, and occasionally a developing picture of so-called chronic pulmonary heart (*cor pulmonale chronicum*). Naturally, in dealing with functional disorders in pulmonary pathology, we speak of the lungs and heart as a single functional system. In cases of chronic fibrocavernous tuberculosis and pulmonary cirrhoses the aspiratory function of the lungs, i.e., external respiration, the initial stage of oxygen intake, is disturbed, being accompanied by retraction of the respiratory pneumoparenchyma associated with deformative growth of connective tissue and destructive processes with cavitation of the lungs. Concomitant changes of the bronchial tree which impair normal bronchial peristalsis, spastic phenomena in the minute bronchi, bronchiectases and emphysematous changes prevent normal aeration. More or less marked reduction of the vital lung capacity is accompanied by an increase of the residual air volume. Oxygen diffusion through the affected membranes is impaired, although CO_2 discharge is affected to a lesser extent. From the very outset, under the effects of toxicemia, there are disturbances in oxygen delivery. However, one should never confuse pulmonary insufficiency and oxygen deficiency. Pulmonary insufficiency is a condition in which the external respiration does not ensure sufficient oxygen saturation of the blood and adequate discharge of accumulating carbon dioxide. Oxygen insufficiency denotes a deficiency of oxygen in the tissues (hypoxia) which may be observed despite normally functioning lungs. On the other hand, the potential compensatory faculties of the body are enormous, so that with a sufficient function of the healthy lung sections, particularly in an unaffected contralateral lung, the oxygen intake, under moderate pressure, may be sufficient to saturate the blood.

Altogether, there are four types of hypoxemic conditions: (1) Arterial or hypoxic; (2) Anemic; (3) Circulatory (congestive), and (4) Histotoxic.

These four types should be considered in choosing cases subject to collapse therapy and surgery and in contemplating postoperative care.

In the clinical treatment of chronic forms of pulmonary tuberculosis involving impairments of external respiration the physician mostly has to deal with combined forms of arterial and circulatory hypoxia. The delivery of oxygen to the pulmonary capillaries is reduced owing to marked anatomical changes of the pneumoparenchyma (sclerosis, reduction of respiratory parenchyma due to cavitation or pneumonia) and impairment of the thoracic respiratory excursions. In addition,

there is a certain degree of circulatory malfunction in chronic pulmonary tuberculosis.

Secondary anemia is observed mainly in irreversible tuberculous cachexia with histotoxic effects too slight to prevent the tissues from assimilating the received oxygen. With further radical surgery, there is always the possibility of acute oxygen deficiency complicating surgical intervention.

According to Van Slyke, the following degrees of hypoxia can be distinguished: (a) first, when blood saturation falls to 89.75 per cent; (b) second, from 87 to 74 per cent, and (c) third, 74 per cent and less.

Hypoxia severely affects the functioning of the central nervous system, and, when especially prominent (e.g., in asphyxia), causes its disruption as well as irreversible changes in the nerve cells. According to V. A. Negovsky, such changes in asphyxia set in after 4 to 6 minutes.

However, as mentioned earlier, chronic forms of pulmonary tuberculosis are mostly associated with chronic manifestations of pulmonary insufficiency which, along with the direct influence of tuberculous toxicemia on the central and vegetative nervous systems, leads to disturbances of such major vegetative functions as sleep and rest. In chronic tuberculosis, recovery from the effects of physical and mental strain is too slow and inadequate. A continuous sensation of fatigue is typical of such patients even in non-febrile periods. Hence the vital importance of air therapy in the general system of antituberculosis measures.

Functional Examination of the Respiratory and Circulatory Organs

Due, on the one hand, to the increasing frequency of recovery and the more benign course of tuberculosis in general, and, on the other, the considerable extension of surgical treatment, there is greater need for a more objective assessment of the functional reserves and compensatory capacity of the respiratory and circulatory organs.

The practicing physician has to assess the degree of loss (limitation) of occupational fitness or, inversely, rehabilitation, and the consequent possibility of return to work. On the other hand, in proposing various modes of treatment, especially surgical, the physician should have a clear notion of the patient's adjustability, and primarily the general state of the integral pneumocardiac functional system.

Functional surveys of the pneumocardiac system in clinical or sanatorium conditions, apart from the common clinical investigations of pulse and breath rate, should incorporate the following: 1. Assessment of disturbances of external respiration by means of (a) spirometry (vital lung capacity, maximal respiratory volume, residual air), (b) measurement of respiratory pause (voluntary apnoe) in inhalation and exhalation, and (c) bronchospirometry for each bronchus (on special indications prior to surgical intervention; to be done clini-

cally); 2. Assays of gas exchange: (a) basic and (b) at rest and after graduated exercise (respiratory volume per minute), oxygen uptake respiratory equivalent, oxygen deficit, etc.; 3. Assessment of hemodynamics (pulse, arterial and venous tension, blood velocity); 4. Electrocardiography.

The enumerated tests and measurements of individual clinical parameters, all indices being expressed as percentages of the values normal for the given age and weight, are utilised to reckon the degree of anomaly in each case, the process being completed with the formulation of a clinico-physiological conclusion. This helps the physician to evaluate the hazards of surgical intervention in every given case and, in solving the problem of rehabilitation, to advise an appropriate choice of working conditions or continuation of specific treatment.

EXTRAPULMONARY SYMPTOMS

Besides considering the possibility of other localisations—lesions to be dealt with in the appropriate chapters—the physician should make allowance for the frequently encountered functional disturbances caused by tuberculous toxicemia. Primarily, these may include reactive manifestations on the part of the central and vegetative nervous systems (neurasthenia, vegetative dystonia), functional circulatory disorders (tachycardia and hypotension), disturbances of the gastrointestinal function-motile as well as secretory (hypochylia, spastic intestinal conditions), etc. As regards the neuropsychic sphere, the increased excitability of the tuberculous patient is a long known fact involving emotional instability, occasionally euphoria and, not infrequently, a tendency to depressive and hypochondriac conditions.

Even in the primary stages there may be marked evidence of fatigability which should be attributed to the effects of intoxication on the endocrine system: the function of the thyroid, pituitary and adrenals. Arterial hypotension is most frequent in the active stage, a return to normal tension corresponding to recovery.

The problems mentioned will be examined at length in the appropriate chapters.

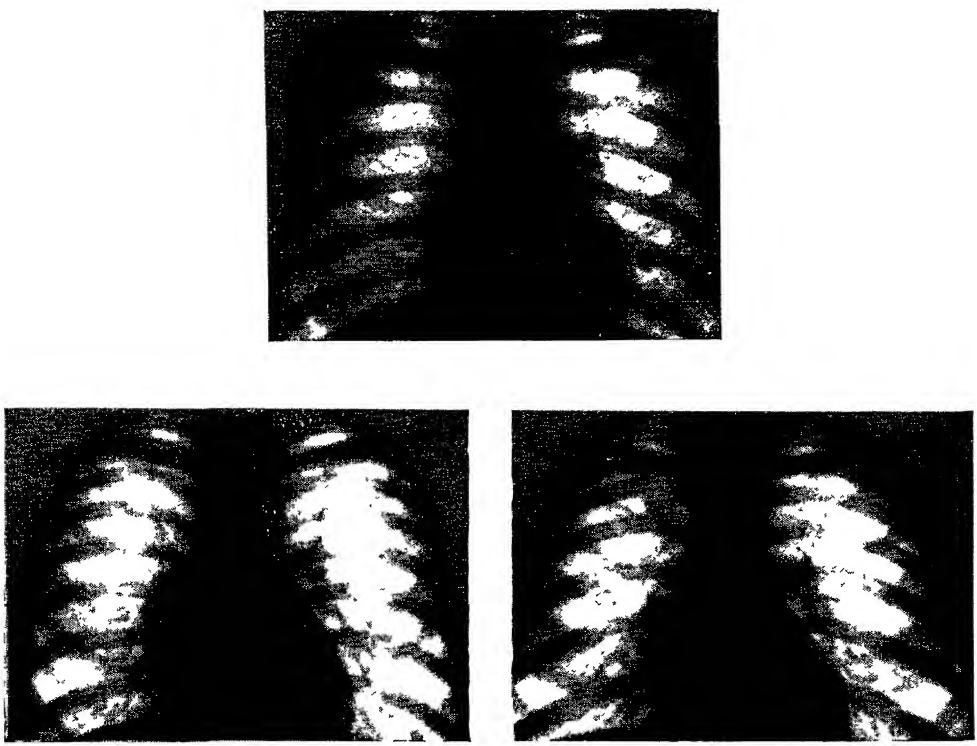


Fig. 23 Large-film fluorograms

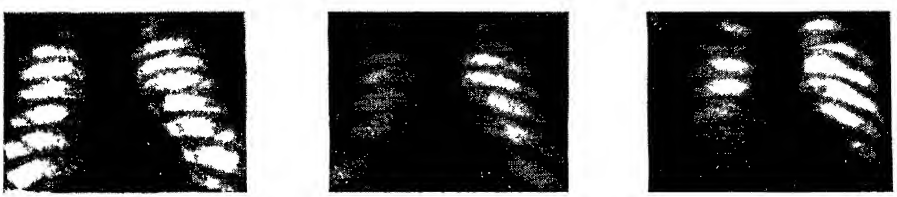


Fig 24 Small-film fluorograms

CHAPTER IV

CASEFINDING AND DIAGNOSIS

Early recognition of incipient signs of pulmonary and other forms of tuberculosis is one of the main prerequisites for effective treatment and recovery. It is achieved, firstly, by adequately organised early casefinding, and secondly, by proper application of up-to-date diagnostic procedures.

EARLY RECOGNITION

Early casefinding must be based on the following considerations:

1. The disease may not have been recognised by the patient,
2. It may proceed with symptoms which camouflage the true cause of the malady (influenza, functional circulatory disorders, dyspepsia, pneumonia);
3. Tuberculosis is an infectious disease, whose initial indications should be sought for in persons living in direct contact with the sources of infection—patients with open forms of the disease;
4. The origin of tuberculosis in adults may often be traced to primary infection in childhood.

These considerations underlie the system of early casefinding in use throughout the Soviet Union. In the first place, prophylactic surveys are carried out among the healthy population by means of screening and lung radioscopy under compulsory radiographic control of all changes revealed. In the everyday practice of out-patient clinics and hospitals, lung X-rays are taken of all applicants and institutional patients, thus forming an integral part of out-patient and in-patient hospital routine. In all cases of expectoration, thorough sputum examination for mycobacteria is imperative. Contacts are subject to periodic examination in antituberculosis dispensaries.

In childhood, particularly in infancy, X-rays should be coupled with tuberculin skin tests to reveal not only clear manifestations of the disease, but also symptomless infection.

The least laborious radiographical method is fluorography, i.e., photography of pictures projected on a fluorescent screen, permitting 50 to 60 cases to be recorded by the small-film, or still better, large-film technique (Figs. 23 and 24). All suspects revealed by prophylactic fluorography are immediately given detailed clinical examination in dispensaries to verify the diagnosis and, if need be, prescribed systematic treatment and follow-up.

Hence initial signs of tuberculosis should be sought among healthy individuals or those who consider themselves so.

Group surveys of the population are the most convenient form of mass examinations. Special surveys are undertaken among child communities, in elementary and secondary schools and institutes, as well as various occupational schools. Other surveys are conducted among such sections of the population as the personnel of children's institutions, schoolteachers, food-processing personnel, pre-conscripts, general medical personnel and, especially, the staff of antituberculosis institutions. The correct choice of population groups for mass surveys is indispensable for success. Special attention should be devoted to the most susceptible age groups, viz., infants, schoolchildren and adolescents. Of course, the infectivity of middle and advanced age should also be remembered, being more frequent nowadays partly owing to increased life expectancy.

In his student surveys, Kattentid found 0.22 per cent of those examined to have active closed forms of tuberculosis, 0.59 per cent so-called border-line forms, and 13.8 per cent, non-active forms of intrathoracic tuberculosis of no practical importance.

From 15 to 17 years of age primary lesions predominate. On the other hand, after 18 there is a prevalence of secondary tuberculosis in its focal, infiltrative and hematogenously disseminated forms.

A marked feature of the system of early detection now operating in the U.S.S.R. is the participation of general medical personnel, primarily local therapeutists of out-patient clinics in the work. The latters' constant co-operation with specialised antituberculosis dispensaries ensures the exhaustive scope and efficacy of early detection.

Bearing in mind the variety of forms tuberculosis may take, particularly pulmonary, and the range of various organic and systemic functional disturbances accompanying the disease, its possible incidence should be considered in all obscure cases and ruled out by differential diagnosis before any definite conclusion is reached.

DIAGNOSIS OF PULMONARY TUBERCULOSIS

Inspection

Diagnostic procedure in pulmonary tuberculosis is not confined to the establishment of etiology and localisation, but should include qualitative assessment of the changes revealed. This can be achieved by consistent and thoughtful application of the classification of pulmonary and other tuberculosis adopted in the U.S.S.R. Clear-cut evaluation of the activity of primary changes in the lungs is especially important.

After taking the history and recording the main complaints, the physician proceeds with external inspection. The general appearance of the patient is often suggestive, but one should always remember that incipient pulmonary changes may not be reflected externally.

Toxicemic effects are most demonstrative in the appearance and general condition of children.

Pallor of the cutanea and visible mucosa can be observed along with emaciation, maldevelopments and nervous hypersensitivity. Tuberculo-allergic symptoms may be apparent as well, including phlyctenulous conjunctivitis (phlyctenes) and *erythema nodosum* which confirm the diagnosis of tuberculosis and are usually, if not always, primary (primary complex, tuberculous bronchadenitis, early generalisation). Surface palpation of the neck along the sternocleidomastoid reveals the multitudes of small indurated lymph nodes so well described by A. A. Kissel.

The adult patient with intoxication demonstrates pallor and, occasionally, lassitude. In febrile conditions, even at subfebrile temperatures, there is an expression of anxiety as in thyreotoxicosis. The skin lacks turgor and vasomotor interplay (red dermography) is observed, along with marked emaciation or wasting. The notorious thoracic cage with wing-like protruding scapula, producing the effect known as *habitus phthisicus*, is of late increasingly less common. In this respect it should be remembered that the *habitus asthenicus* observed in people with a drop heart and fluctuating X rib, at one time described by Stiller, is not the result of tuberculosis, but mostly an individual constitutional feature.

Sparing of one side in breathing, which the patient may not even notice, is observed not only in connection with inflammatory changes in the lungs and pleura, but also in atelectasis. Protrusion of one of the sections of the thorax is sometimes noted in pleurisy with effusion. A semi-immobile, rigid thorax, scarcely altering its outline, is revealed in pulmonary emphysema.

In cases of circulatory obstruction in the lesser circuit or when the mediastinum is displaced to the left, there may be varicosity of the thoracic cutaneous veins. Thorax palpation occasionally reveals increased resistance and pain in cases when the process has involved the parietal pleura. On a number of occasions, hyperesthesia may be noted when testing the sensitivity of the cutanea. It is advisable to augment inspection by measuring the thoracic volume with a cyrtometer. Weekly measurement of weight is imperative.

Percussion and Auscultation

Finger percussion and especially auscultation have retained their significance despite the advent of radiology. A combination of physical and radiological examination provides more accurate data on the condition of the thoracic organs and especially the lungs.

Radiological control led to the abandonment of certain erroneous interpretations of percussional and stethacoustic findings. Thus, for instance, a slight impairment of the percussion noted above the right apex is sometimes merely the result of more extensive development of the right muscles of the shoulder girdle. The same refers to the

cases of harsh breathing in the right apical area accounted for by the position of the subapical bronchus.

A boxy (hypersonorous) tympanic sound may be caused by emphysema, limited by the induction of pneumothorax, or by a large smooth-walled cavity. The best method of differentiation in such conditions is radioscopy, which is far superior to auscultation and percussion, all the more so since the classically described sound changes obtained after Wintrich at percussion of suspicious areas with an open or closed mouth or, after Gearhart, in different positions of the body, are seldom encountered.

Lung thickening evidenced by impairment or flatness is readily detected by percussion, having the radiological appearance of a shadow. Such changes are observed in pneumonia, infiltrates and atelectasis. Radiological and physical findings should be assessed under mutual control.

Changes in the aeration of the pneumoparenchyma are revealed by comparative (staccato) percussion of symmetrical areas of the thoracic surface. The contours of a flatness are best traced by deep, palpatory percussion.

The apices are sounded by paraclavicular percussion. The difference in the degree of aeration or, rather, in the degree of flatness between the right and left apices, becomes clearer with the use of comparative percussion in inhalation and exhalation.

Moist small-sized or, less frequently, medium-sized rales observed in infiltrative changes and bronchopneumonia mostly indicate an active process which, however, is not true of the peculiar slightly cracking rales which denote sclerotic pulmonary changes or cirrhoses. In F. G. Yanovsky's well-justified opinion, large-sized rales, especially the resonant variety, always bespeak a destructive (cavitary) process.

Dry rales are commonly associated with concomitant bronchitis or, occasionally, spastic (asthmatic) symptoms in the bronchi. Very often the lungs reveal areas with limited dry rales which accompany perifocal inflammations involving both the pneumoparenchyma and the bronchial airways within the limits of one or several segments.

Special note should be made of pleural phenomena, such as a pleural friction sound which becomes louder when the stethoscope is pressed to the thorax. In contrast to catarrhal changes, the pleural friction sound, occasionally resembling crepitation, is heard during inhalation and exhalation.

Auscultation should be done methodically, first assessing the rhythm and rate of respiration and then the catarrhal manifestations.

At normal deep and regular respiration moist rales are not always detectable, being more audible with a slight cough. After this the patient is asked to take a deep breath at the level of which moist rales may be heard in cases of infiltrative, bronchopneumonic or cavernous changes (Fig. 25). Naturally, there are no rales pathognomonic for tuberculosis.

The existence of catarrhal manifestations or dry or moist rales

mostly indicates an active process. A smaller incidence and total disappearance of rales established in regularly repeated examinations are a propitious symptom indicating quiescence and stabilisation and, if combined with a stable absence of catarrhal phenomena and other clinical findings, denote recovery.

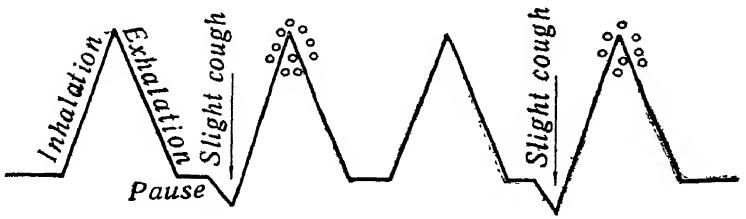


Fig. 25. Diagram of lung rale auscultation after slight coughing

There is a further essential point to be considered. In certain cases not only the initial tuberculous foci but even cavities may be undemonstrable stethacoustically. Such cavities are usually referred to as silent. We personally uncovered them in 18 out of 354 patients with cavities. Silent cavities are now met more frequently than before, since chemotherapy tends to decrease catarrhal manifestations, making them disappear more rapidly, and, besides, in certain cases cavities undergo cystous transformation and their walls heal. For convenience in subsequent examinations, the stethacoustic and percutory findings are plotted symbolically on a simple chart (cliché) of the thorax or lung fields (Fig. 26) in accordance with the topography of the revealed changes.

Auscultation is best done with a wooden stethoscope, but in general practice it is more convenient, of course, to employ a binauricular phonendoscope.

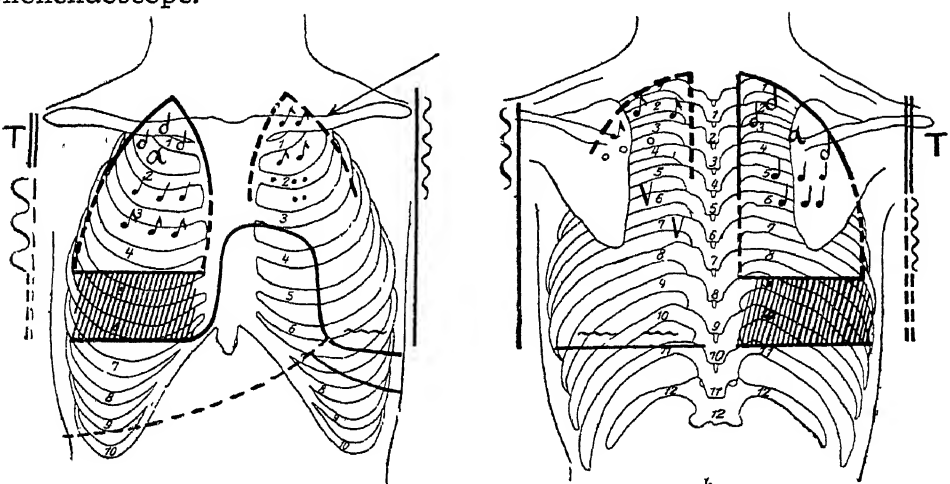


Fig. 26. Symbols for recording physical findings (after Ulrici)
(a) anterior, *(b)* posterior

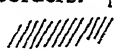
Radiology

The importance of radiological examination cannot be overestimated. At present, it includes orientational, surveillant and directed radioscopy, radiography and tomography (laminography). The competent use of these methods in indicated cases offers the physician important data for correct diagnosis. Final diagnosis, however, remains the function of all-round clinical study.

Radiological findings do not, of course, enable conclusions to be reached on the etiology and specificity of the process. The radiological method may be used to pinpoint the site of the lesion in the organ, as well as its size, special features (thickening or softening of pulmonary tissue) and topography.

SYMBOLS FOR RECORDING PHYSICAL FINDINGS (AFTER I. ULRICI)

1. Percussion

Flatness: part of the lung field demarcated by an uninterrupted line
Impairment: dashed outline
Tympany: the letter *T* beside the tympanic area
Reduced mobility of lung borders: + + + +
Exudate: hatched area 

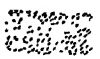
2. Changes of Respiratory Sounds

Recorded by lines of required length beside thorax:

- Increased: uninterrupted line
- Reduced: dash line
- Absent (breathing not transmitted): double dash line
- Vesiculobronchial: fine zigzag line
- Bronchovesicular: large zigzag line
- Bronchial: double uninterrupted line
- Harshness: noted on the margin
- Amphoric: noted on the thorax at the point in question

3. Bronchitic Rales (Dry): multiple symbols within thorax
Pleural rubs—at respective point of diagram

4. Rales

Crepitant –  Number of rales denoted by number of symbols

Moist (large-sized, medium-sized, small-sized)  Sonorous moist rales denoted by musical symbols.

5. Special Findings are noted on the margin

These symbols are simple and convenient and offer a clear idea of the results of physical examination. Standard high-quality equipment is indispensable for correct radiological conclusions, being especially vital in comparative dynamic examination, i.e., the comparison of documentary data, in the first place serial radiographs referring to various stages of the disease.

Apart from orientational and directed radioscopy, initial examinations should always include radiography, the X-ray film being more sensitive than the eye. Many cases are known, for instance, of radiography revealing shadows with a diameter of 1 to 2 millimetres, while radioscopy proved futile.

Lung Radioscopy

In comparing the density of shadows in radioscopy and radiography, it is useful to apply the d'Abreu scale, which distinguishes shadows: (1) less dense than the costal; (2) similar to the costal; (3) similar to the clavicular; (4) similar to the heart shade; (5) cardiocostal; (6) similar to the shadow of the liver.

The degree of contrast between the aerated tissue and thickened or softened areas forms a basis for evaluation of individual radiological pictures.

In radioscopy—the functional stage of radiological examination—we see the thoracic cage and its organs in motion: the contracting heart, the rise and fall of the lungs with their respiratory volume altering at inhalation and exhalation, the diaphragm rising at inhalation and descending at exhalation, and the ribs changing their position according to respiratory movements. Normally, we see the hilum and the tree-like pattern emanating from it, mainly accounted for by the ramifications of various vessels (*a. pulmonalis*) showing against the background of more or less transparent air-filled parenchyma.

It is essential to note that radioscopy permits the lungfields to be examined in various directions (multiaxial radiology after A. Y. Prozorov). As a rule, radioscopy is done under dorso-ventral or ventro-dorsal illumination, in profile, and in the first or second oblique positions (with the right or left shoulder respectively forward).

Oblique and profile radioscopy offers visual access to the anterior and, chiefly, posterior mediastinum. In a number of cases it provides a better view of clustered lymph nodes, tumour-like formations, interlobar exudates, etc. Radioscopy affords a clear picture of changes and deformities of the diaphragmic cupolas, pathologically retarded respiratory movements and paradoxic movements of a paralysed diaphragm (upward in inhalation and downward in exhalation).

Radioscopy affords a good view of mediastinal displacement and pathological fixation.

In directed radiology different devices are employed to obtain a better view of various pulmonary segments. So, the apices are seen

well in Gassul's position, the patient standing with his back to the screen in a low bow facing the tube, the neck stretched forward and the chin raised. In this position the projection of the superior lung aperture is enlarged and the suprathoracic parts of the apices become more easily visible. To inspect the infraclavicular zone, the patient's hand is raised, thereby lifting the clavicle as well.

Lung Radiography

As we know, examinations of tuberculous patients cannot be limited to radioscopy, but should always be augmented by radiography. Radiographs of the lungs taken during aspiration within 1.2 to 2 metres from the tube focus, produce the most clearcut unmagnified pictures. The voltage should range between 90 to 100 kV, with exposure lasting several tenths of a second.

In the U.S.S.R., use is made of bilateral films with a sensitivity of 200 units and a standard size of 30x40 for adults and 20x30 for children.

Lung X-rays are taken in different directions in accordance with special indications established by radioscopy. They may be taken dorso-ventrally or ventro-dorsally, in the first or second oblique positions, or, more often, in profile. Laterography, i.e., X-rays taken with the patient lying on his side, is employed in cases of mobile exudate in the lungs.

Interpretation of Normal and Pathological Radiographs

Radiographs are examined on film-viewers or against daylight.

The examiner first notes the position of the heart, the condition of the thoracic skeleton and the outline of the diaphragmic cupolas, then methodically scans the lung fields and hilus in the craniocaudal direction. In studying the density of the lung pattern, one should remember that it tends to decrease gradually from the hilus to the periphery, whereas in the cortical areas it is hardly visible. The hilar shadow normally varies depending on the subject's physique—athletic, asthenic, pyknic or mixed.

The topography of the lymph nodes is well presented in Sukennikov's diagram (Fig. 27). Normally, the lymph nodes charted on the diagram are invisible both radioscopically and radiographically. Pathologically affected lymph nodes are revealed in the respective positions either after massive caseation when they are fused into clumps, or still more clearly, when calcified. In dorso-ventral radiography, the massive congregation of hilar vessels mostly overshadows all minimal lymphatic lesions except those which have been calcified. A final conclusion may be drawn only after oblique and profile radio-

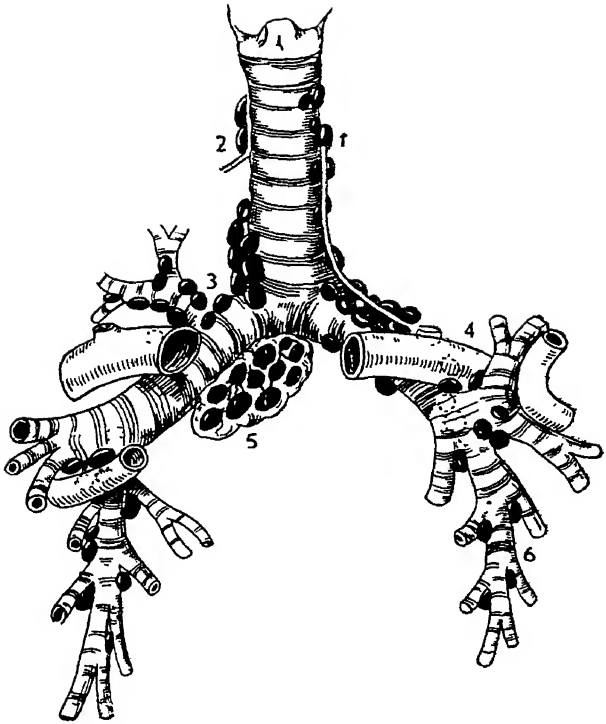


Fig. 27. Topography of bronchial glands (after Sukennikov)

(1) Lymphoglandulae tracheales sinistrae; (2) Lymphoglandulae tracheales dextrae; (3) Lymphoglandulae tracheobronchiales superiores dextrae; (4) Lymphoglandulae tracheobronchiales superiores sinistrae, (5) Lymphoglandulae tracheobronchiales inferiores; (6) Lymphoglandulae bronchopulmonales

graphy which afford a view of the posterior mediastinum (Fig. 28, *a* and *b*).

In pulmonary disease we may encounter two basic processes: either the pneumoparenchyma is congested as in pneumonia and atelectasis (A. Y. Prozorov), productive inflammation and sclerosis, or there is destruction of the lung tissue. In both cases the described lung pattern undergoes drastic changes which may be limited, as in focal lesions, or diffuse, as in generalised changes involving an entire lobe or lung.

Radiographically, consolidated lung tissue appears as focal, strand-like or diffuse shadows of varying density. Focal shadows may be either limited and strictly localised, or disseminated over large areas of the fields, occasionally occupying their entire surface. They range from a millet grain and pea in size to large conglomerates. The shadows may vary in intensity from well-outlined and sharp, as in calcified lesions, to slight, hazy-contoured cloud-like formations correspond-

ing to infiltrations. Productive foci are radiographically less dense than petrifactions, but are more massive and more clearly outlined than infiltrations. Softer nodular shadows are occasionally observed in symptoms of congestion in the lesser circuit. Atypically arranged fibrous cords often extend from the hilus to the interclaviculo-hilar and hilar regions, covering either limited areas or large portions of the lung. Diffusely disposed strands may sometimes be associated with lesser circuit congestion in which the hilar shadows are broad and extremely massive. In other cases the incidence of strands is linked with perivascular and peribronchial lymphangoitic scleroses, which are frequently an immediate or remote concomitant of a primary complex.

The types of intensity enumerated may occasionally be obscured by the shadows of pleural superimpositions, although there are cases when pleurisy is complicated by strands and annular shadows causing considerable difficulties in interpretation.

Apart from the above, we may mention the earlier discussed cases involving loss of tissue, mostly related to cavitation. Here radiography shows a more or less circumscribed translucency located in healthy or pneumonically changed lung tissue or, occasionally, in areas of more or less pronounced fibrosis. In the first case the cavity has not yet become organised (early stage), lacking a developed wall (capsule). In the first and second instances, the cavity is in the process of organisation, being walled off from the surrounding tissue by an annular capsule (advanced stage). Cavity walls are particularly massive in cirrhoses. The lung pattern in the translucent area is less intense or even totally invisible as, for instance, in large cavities. Occasionally, the horizontal surface of the liquid content is seen at the bottom of a cavity. In some cases even large cavities do not show up in radiography because they are hidden by massive apical caps (pleural superimpositions) demonstrable by the common physical methods and especially by tomography (Fig. 29, *a* and *b*).

Bronchiectatic cavities, often disposed about the hilus, at times look like honeycombs. Occasionally, they are much larger, but conventional radiography may prove inadequate for diagnosing ectasis. In such cases liquid contrast matter (lipiodol) is introduced intrabronchially, filling in the cavities and producing a vivid picture of the changes. At times, as, for instance, in emphysema, an entire lung field or individual segments appear as a diffuse translucency. A total absence of the lung pattern over limited areas or entire fields is noted in pneumothorax, the ribs being seen in negatives against a dark background. With an artificial pneumothorax, it is important to take note of the respective positions of the lungs on the screen and radiograph during inhalation and exhalation. This helps to work out the prospects of collapse (maximum collapse during exhalation) and discover hitherto unnoticed adhesions. The lung pattern may conceal exudate in the pleural cavity. If, besides exudate, the cavity contains gas, the exudate is demarcated by a horizontal line which shifts at

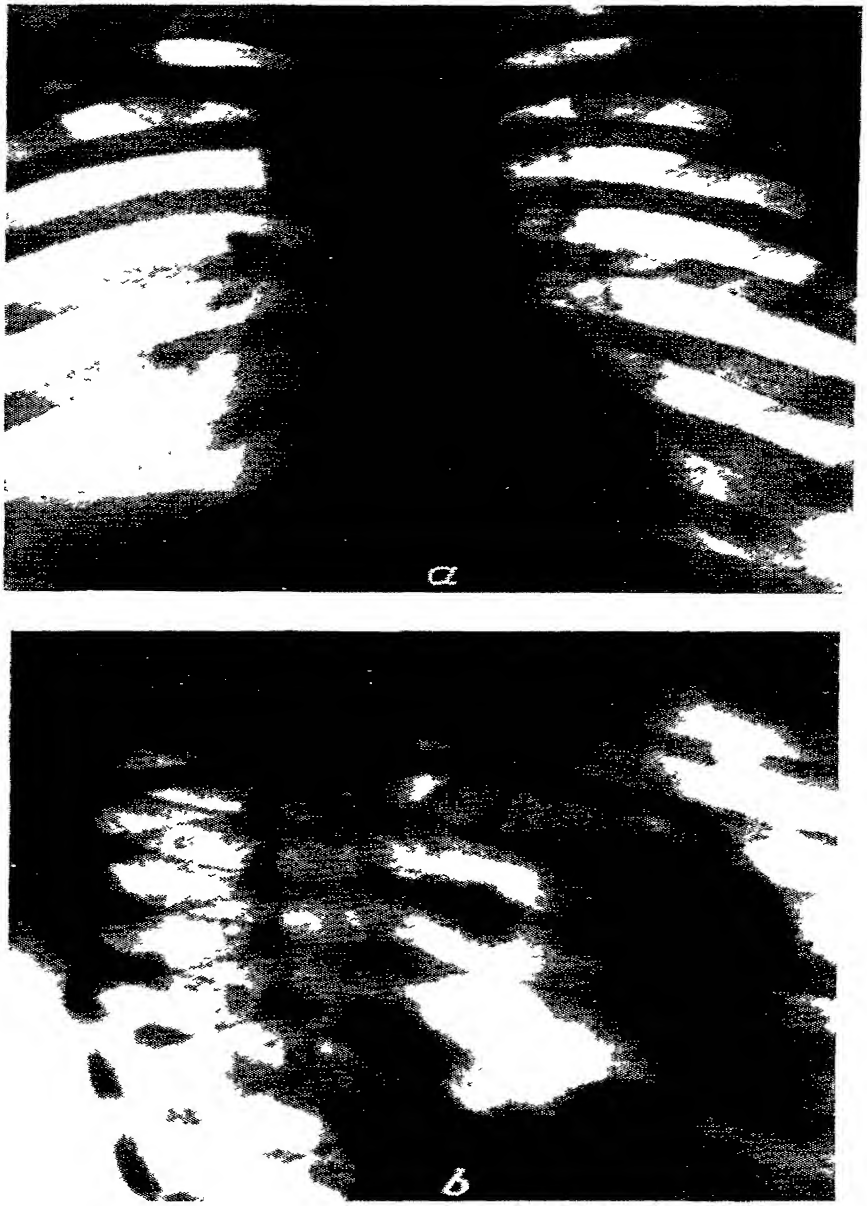


Fig. 28. Tuberculous bronchadenitis

(a) tuberculosis of the bronchial and paratracheal lymph nodes (seen dorso-ventrally), *(b)* the same diagnosis in laterography, clusters of indurated and calcified glands in the retrocardiac space

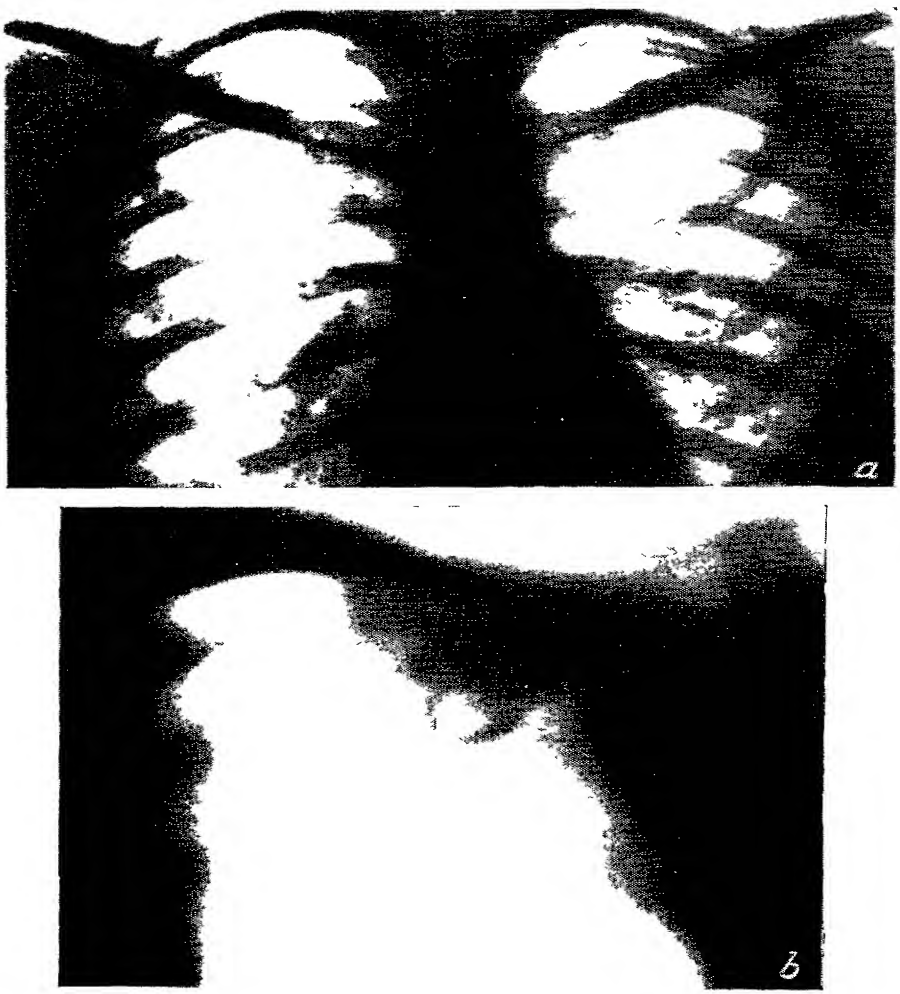


Fig. 29 A cavity in tomography
(a) cavity undemonstrable radiographically, *(b)* the same case cavity well discernible on tomogram

every change of position (seropneumothorax, pyopneumothorax, etc.). Pictures associated with interlobar pleurisies and the subsequently emerging strands are especially vivid. Radiology is of great help in diagnosing paramediastinal pleurisies and lesions of the lingula. Also of use in pneumopleurisies is laterography—with the patient lying horizontally on the healthy side. This makes it possible to reveal the topography of the adhesions which in the conventional position are obscured by exudate.

Limitations of Radiological Examination. Diagnostic Errors

Biased assessment of radiodiagnostic findings may lead to faulty conclusions. In many respects, a great deal depends on technique. Barring gross technical defects, it should be borne in mind that soft photographs contain too many details of the lung pattern which may be erroneously interpreted as pathology. Excessively hard pictures are too transparent, obscuring details. Poor radiographical fixation of the thorax produces hazy lung patterns and focal pictures. The same results from overexposure. The picture is clearer at short exposures of from 0.1 to 0.2 seconds.

The density, chemical composition and arrangement of foci, of course, affect the clarity of the picture. Calcified foci are usually sharply demarcated from the surrounding parenchyma, but small fibrocaseous areas may produce almost identical pictures. It should be remembered that a radiograph reflects lesions and changes of different depth projected on the same plane. Hence, the shadows may be superimposed on each other. The diagram in Fig. 30 demonstrates the value of tomography in correcting such faults.

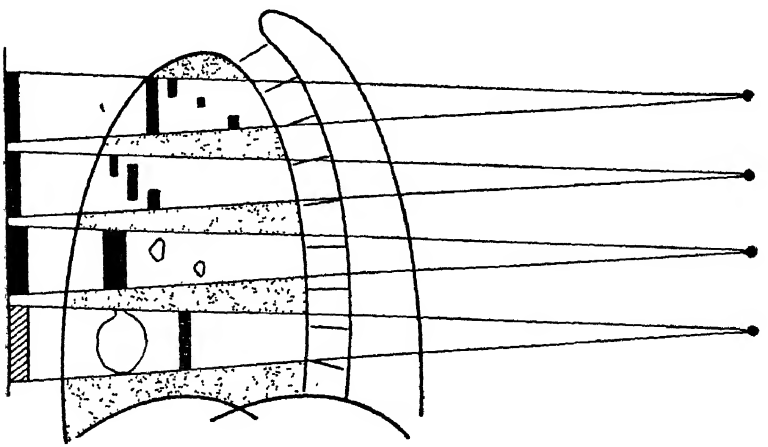


Fig. 30. Summation and superposition of changes producing radiographic densities in sagittal plane

Pulmonary changes	Thorax Inspection	Percussion	Auscultation (breathing)
Normal lung (aerated)	No anomalies	Pulmonary sound	Vesicular
Excessive aeration (emphysema)	Distended thorax and reduced respiratory movements	Boxy sound (tympanic)	Reduced
Partial and limited thickening	Occasional moderate lag of corresponding thoracic section	Flatness over limited area	Indefinite, in some cases harsh or vesicular
More widespread thickening (infiltration, pneumonia)	More pronounced lag of afflicted side at respiration	Dullness, sometimes with a shade of tympany	Broncho-vesicular or bronchial
Softening of pneumoparenchyma in cavities	Lag of affected side at respiration	In fresh and minimal cavities sound changed slightly, at more marked flatness has a tympanic shade	Bronchial, sometimes amphoric
Pneumothorax	Occasionally, slight protrusion of thorax, lag of afflicted side	Tympany	Reduced or mandible
Pleurisy with effusion	Lag of afflcted side at respiration	Dullness, tympany in overlying area	Reduced or mandible

Physical and Radiological Findings

Rales	Radiography	Tomography	Respiratory function
None	Normal lung pattern		12 to 16 respirations per minute
With concomitant bronchitis dry	Excessive aeration of lung		Accelerated to varying degrees
Dry, medium- and small-sized moist rales (bronchopneumonia)	Limited clustering or homogeneous density. Lung pattern retained in affected sections	Focal densities more clearcut and more massive than in radiography	Accelerated, especially at temperature rises
Moist rales of varying character, sometimes sonorous	Marked density of segments or lobes	More pronounced density, occasionally with destructive changes	Depending on extent of lesion
Large-sized, often sonorous moist rales, especially after coughing	Limited transcendencies with various types of cavity walls (infiltrated, fibrous, bullous), annular shadows, often with draining bronchus	In some cases cavitation is indiscernible in radiography, and revealed only tomographically	Depending on extent of lesion
Absent or damped	Excessive transluceness of lung field, limited by retracted lung section. Vascular pattern indistinguishable		Accelerated during adjustment
Pleural friction heard initially and after resorption	Homogeneous density over lung field, sometimes limited by Damoiseau's line		Accelerated due to compression or febrile syndrome

Tomography

Tomography (laminography) is used to obtain series of pictures at a pre-set depth usually measured from the spine. Tomographs are obtained by the use of special vertical or horizontal tomographic cameras.

The operating principle of the camera comprises the use of a pendulum rotating around its axis, with the X-ray tube attached at the latter's top and the film cassette at its bottom. When the pendulum moves vertically, the camera produces clear-cut pictures of foci or other changes localised in the respective lung stratum. Usually 4 to 6 pictures (sections) are taken at a distance of 1 to 2 cm from each other. If necessary, the number of pictures may be increased and the intervals reduced. To minimise exposure to diagnostic radiation, so-called simultaneous cassettes are used in which all the required layers are photographed at the same time.

Tomography represents a better means of locating the lesion, tracing its outline or revealing a focus not reflected in previous conventional radiography owing to an obscuring shadow. Tomographic series are invaluable in detecting cavities, e.g., fresh cavities not found on a conventional lung X-ray or concealed in an atelectatic area, etc. In a number of cases tomography literally provides a key to a survey X-ray.

Tomographic facilities should be available for control during treatment, convalescence and follow-up. It cannot be said that cavity healing has taken place unless it has been confirmed tomographically. Estimations of residual lung changes should likewise be substantiated by tomography.

It is extremely important to compare the findings of examination by different methods.

Bronchography and Tomobronchography

Bronchial changes and bronchial obstruction play an important part in the emergence of pulmonary pathology. Bronchites, bronchiolites, and occasionally, lesions of the bronchial wall accompanied by bronchial deformation with the rise of bronchiectases and bronchial stenoses, may emerge in etiologically different pulmonary conditions.

Apart from that, the emergence and development of tuberculous cavities is most closely bound with pathological conditions of the bronchi (draining bronchi in particular).

It is extremely important to make a thorough comparative analysis of data obtained by different methods of examination, in particular, radiographs and tomographs taken with the use of contrast medium (lipiodol) filling in the bronchial system.

CHAPTER V

CLINICAL LABORATORY STUDIES TUBERCULIN SKIN TESTS

In every individual case the scheme of laboratory investigation is selected by the physician, but it must always include comprehensive examination. The main lines of examination are macro- and microscopy of sputum and other secretes, i.e., pus from fistulae, pleural exudates, etc.

SPUTUM EXAMINATION

The examination of properly collected daily sputum consists of:

1. Assessment of daily amount and macroscopic picture: purulent, mucous, mucopurulent, sand-like (*Actinomyces*), incidence of blood streaks;
2. Microscopy of direct smears;
3. Bacterioscopy for *Mycobacterium tuberculosis*;
4. With negative bacterioscopy—concentration;
5. Bacteriological study for *Mycobacterium tuberculosis* through cultivation on solid yolk media *in vitro*;
6. With negative cultivation results—biological tests: injection of suspicious material into guinea-pigs.

Biological tests (guinea-pig inoculation) are usually the most sensitive. Occasionally, when checking convalescents after treatment with phthivazid and related drugs, animal inoculation may produce negative results accounted for by the drug-resistance developed by the given microbe specimens and the consequent reduction of their virulence.

To confirm pneumoparenchymal disintegration, direct smears are examined for elastic fibres, the character, cellular content, etc., of the sputum being noted simultaneously. In addition, for purposes of differentiation, the smears are put to careful cytological examination for cellular elements, e.g., malignant neoplasmic cells. A Giemsa-stained preparation is tested for eosinophils in bronchial asthma or, occasionally, in eosinophilic pneumonia.

When there is no expectoration, the examination is made from laryngeal swabs, on bronchial lavage after Y. S. Zobin, or on gastric lavage after Armand-Delille.

Microscopic technique. To prepare samples, the sputum is poured into Petri dishes, firm purulent clots being picked from different places with a preparing needle and put on 3 to 5 slides. One slide is closed with a cover-glass to study fresh sputum. On the rest of the slides the sputum is spread with a slide or needle. The samples are fixed in a burner flame and stained (after Ziehl-Neelsen or Spengler).

Direct smear microscopy. In microscopy, note should be made of: (1) cell elements such as leukocytes, red blood cells, etc.; the presence of alveolar epithelium shows the sputum to have come from the lungs and not the upper airways; (2) tissue elements.

Staining after Ziehl-Neelsen. A fixed sample is stained with Ziehl's fuchsin, rinsed with water and decolorised with 3 per cent hydrochloric acid alcohol which produces a greyish colour, then again washed in water. The process is completed with methylene blue applied for $^1/_2$ to 1 minute and washing in water.

In the resultant preparation *Myco. tuberculosis* stain red and are clearly discernible on the blue background. The formed elements—leukocytes, epithelial cells and vulgar flora—stain blue.

Spengler's technique (modified). The swab is fixed in a burner flame, then stained with Ziehl's fuchsin in the following way: the fuchsin is poured on the sample which is covered with filter paper; the preparation is then held in a burner flame until the appearance of vapour and washed with water. Then it is decolorised with a solution of 3 per cent hydrochloric acid alcohol and rinsed in water, after which it is stained in picric acid and again rinsed in water. After staining in this way, the sample's background and tissue elements become yellow and the tubercle bacilli stain red.

Bacterioscopy. Stained samples are examined whole. If bacilli are present, their approximate number is counted, noting the result as follows: "10 to 20 at each view", "microbes seen at occasional views", "solitary microbes in sample". Before stating negative results, several samples are usually prepared and tested.

Luminescent Bacterioscopy

In recent years, the method of luminescent or fluorescent microscopy has been adopted in bacteriology. The writer personally employs the following techniques. Conventionally prepared samples of the pathological material are fixed in flame and submerged in a mixture of 0.01 per cent rhodamine and 0.1 per cent auramine taken in equal parts. The stains are heated till vapour appears, decolorised in 3 per cent hydrochloric acid alcohol for 2 to 3 minutes, thoroughly washed in water and dried. The dry samples are examined in a luminescent microscope or conventional instrument fitted with a special device for luminescent microscopy. The simplest device consists of a powerful light-source, a blue light filter on the latter and a yellow filter on the eye-piece.

The use of luminescent microscopy facilitates and quickens the detection of tubercle bacilli, since inspection is done by the dry technique with low magnification. This considerably widens the field of vision which accelerates inspection.

In addition, on the dark field background afforded by the sample bacilli emitting a golden fluorescence are clearly seen and easily detected. Unfortunately, bacillary structure, length and acid-fast granules are indiscernible in this method, which somewhat limits its possibilities.

Concentration

The sputum is placed in a narrow-necked flask of 200 to 250 ml capacity so as to cover only the bottom. An equal volume of 0.5 per cent alkali is added to liquid sputum (double the quantity if the sputum is thick), thus producing a homogeneous substance. The flask is then shaken for 10 minutes, and approximately 50 ml of distilled water with 1 ml of a hydrocarbon (toluol, xylol, petroleum) is added; another portion of distilled water is poured in to half the flask's volume, whereupon the whole mixture is shaken until a fine suspension is obtained. Then the bottle is filled to the neck with water and left to stand for not less than two hours. The suspended mycobacteria, impelled by the hydrocarbon particles, come to the surface, forming a ring-like layer. After two hours the upper layer is removed with a sterile pipette with rubber syringe and repeatedly deposited in drops on slides placed on a boiling water bath. Then the samples are stained (after Ziehl-Neelsen) and put to microscopy. Concentration is 15 to 17 per cent more effective than direct smear microscopy and only a little less sensitive than cultivation.

Cultivation of Sputum and Other Pathological Material for Mycobacterium Tuberculosis

In cases when repeated analysis fails to reveal bacilli in the sputum or other secretions (urine, exudate), diagnosis or therapy check-up (for efficacy of drug treatment or artificial pneumothorax) is carried out by cultivation in artificial media. The method comprises preliminary treatment of sputum and other pathological material with 5 to 10 per cent sulfuric acid or 8 per cent sodium hydrochloride to remove all commensal microflora. If the material (urine, sputum, exudate, etc.) does not contain microflora or shows a small quantity of non-alkaline-fast coccal flora, treatment with 8 per cent alkali will suffice. If the material (feces, urine, animal viscera) is highly contaminated, especially with bacillary flora (*B. coli*, etc.), it should be treated with 5 to 10 per cent sulphuric acid, in which the acid- and alkaline-fast tubercle bacilli retain their viability. The sputum is homogenised during 15 minutes with a double volume of 8 per cent alkali in a sterile vessel with beads, then centrifuged for 5 minutes, the resultant sediment being neutralised with 50 per cent

hydrochloric acid and inoculated into 5 to 8 test tubes containing yolk media (Petragnani, Gelberg, etc.). The test tubes are sealed with wax and paraffin left for 3 months in a thermostat at 37.5 to 38°C. In most cases, the first colonies appear on the 18th, 20th or 30th day of thermostat maintenance.

Preparation of Petragnani medium. The eggs are washed with a brush in warm water and soap and put into alcohol for one hour Ten eggs require 250 ml milk, 16 g starch and 1 g peptone. The starch and peptone are mixed in the milk and cooked for one hour on a boiling water bath with beads, the mixture being stirred frequently. The obtained jelly is cooled to 50 to 60°C after which the eggs are broken into it (8 whole eggs and 2 yolks). The substance is then mixed thoroughly. After that 24 ml of sterile glycerine and 15 ml of a 2 per cent solution of malachite green are added. The entire mixture is strained through a funnel with a gause filter and poured into test tubes. The test tube content is inspissated, the medium being put to curdle in a Koch oven for one hour at 87 to 90°C. Since after curdling no condensation liquid is left in the medium, 0 5 ml of Soton's medium containing 25 units of penicillin per ml is deposited with a sterile pipette in each test tube. The tubes with the medium are tested for sterility by placing them in a thermostat for one hour. Due to the short time during which the medium remains sterile all manipulations should be done with strict aseptic precautions All vessels used for preparing the medium should be absolutely sterile.

Bronchial Lavage

The study is made on fasting subjects after Y. S. Zobin. A 10 per cent solution of cocaine is used to anoint the root of the tongue, glottis, laryngeal walls, Morgagni's ventricles and the exterior parts of the larynx. To obtain washings from an individual bronchus the patient is put in a suitable position on his side. After 3 to 5 minutes, saline is introduced into the glottis by means of a laryngeal syringe, the tongue being drawn out so that the patient does not swallow the saline. The bronchial content is expectorated into a sterile vessel and tested by concentration or cultivation.

As regards its sensitivity, lavage bacterioscopy reveals bacillarity in 9 per cent more cases than microscopy of direct smears. Cultivation of lavage on solid media reveals an additional 10 per cent, i.e., altogether the method produces 19 per cent additional findings.

Gastric Lavage

(After Armand-Delille)

A fasting patient is given a drink of 200 ml of a 1 per cent soda solution (in distilled water), after which the gastric lavage is obtained by a stomach tube. The sample is collected in a sterile vessel and tested by concentration or centrifuged, the sediment being cultivated on artificial media.

EXAMINATION OF EXUDATE AND PUS

When examining the content of serous cavities, punctates from closed abscesses and other matter, the absence or presence of post-

primary infection must be determined. For this sterilely obtained material is inoculated into conventional media (sugar broth, Tarozzi's broth or meat-peptone agar). The flora developing in the media is tested additionally for pathogenicity and drug-resistance.

Exudate tests for tubercle bacilli are made by microscopy of direct smears stained by the Ziehl-Neelsen or Spengler techniques, and by cultivation on egg media.

The non-curdling serous exudate obtained from serous cavities and the spinal channel are centrifuged, the sediment being treated by the conventional procedure and cultivated for tubercle bacilli. Purulent exudate obtained from the pleural cavity as well as pus from abscesses, etc., is put into a glass vessel with beads to be cultivated for tubercle bacilli without preliminary centrifugation.

Studies of protein content and cellular composition are an indispensable part of all exudate tests.

Protein content is determined by the Brandberg procedure as with urine, but the dilutions are greater in accordance with the higher protein content.

As stated earlier and described in the respective sections, examination of various materials and, especially, sputum for tubercle bacilli should be made extremely meticulously. A negative result may today be scientifically confirmed only after the entire round of studies: repeated bacterioscopy of stained samples, concentration, cultivation on artificial media, and, finally, guinea-pig inoculation. In common practice, however, this is not always applicable. Therefore, it is necessary to make repeated studies of sputum and other materials with simultaneous inspection of sample series prepared by concentration or sedimentation.

In modern antituberculosis treatment with the predominance of drug therapy isolation of tubercle bacilli from the pathological material is necessary not only for diagnosis or control of therapeutic effects, but to determine the properties of the bacilli in the given patient, such as virulence, catalase activity and, chiefly, susceptibility to the basic drugs producing an etiotropic effect in tuberculosis —streptomycin, phthivazid and P.A.S.

DETERMINATION OF DRUG-RESISTANCE

The drug-resistance of tubercle bacilli is determined by the use of serial dilutions. A suspension of *Mycobacterium tuberculosis* is prepared containing a definite quantity of microbe cells, viz., 500 million per ml, by optical standards. One ml of the suspension is inoculated into a number of test tubes containing different concentrations of chemotherapeutic drugs.

The purpose of the test may be served by liquid as well as solid media, provided that the medium is sterilised before adding the drug to prevent the latter's inactivation. The results of the test are asseyed on the 12th to 14th day. The highest drug concentration permitting

the growth of a strain indicates the degree of its resistance, and the lowest concentration preventing growth, the degree of its sensitivity.

Streptomycin-resistance is measured with concentrations of 500, 100, 25, 10 and 1 γ/ml.

Strains which grow at concentrations of 100 γ/ml and more are considered highly-resistant; those growing at 10 and 25 γ/ml medium-resistant, while those that reveal growth at lower concentrations are said to be sensitive. Phthivazid sensitivity is tested at concentrations of 100, 20, 10, 1 and 0.06 γ/ml.

With regard to other drugs of the hydrazid group, their activity is greater, the strains termed as highly-resistant grow at concentrations of 10 γ/ml and more, medium-resistant from 1 to 10 γ/ml and sensitive strains at concentrations less than 1 γ/ml.

Strains growing at concentrations of 25 γ/ml and more are considered highly resistant to P.A.S. from 10 γ/ml medium-resistant and from 1 to 10γ/ml sensitive.

CATALASE ACTIVITY OF MYCOBACTERIUM TUBERCULOSIS

Like other aerobe microbes, *Mycobacterium tuberculosis* produces the ferment known as catalase which plays an important part in the vital activity of the microbial cell. Mycobacteria resistant to isonicotinic acid hydrazides undergo profound changes involving a whole number of the microbial metabolic processes. In particular, they lose the ability to synthesise catalase and decompose hydrogen peroxide—a toxic product of bacterial metabolism (Middlebrook, 1954).

The loss of catalase activity by mycobacteria resistant to the isonicotinic acid hydrazides, is usually accompanied by a sharp reduction of their virulence for guinea-pigs. At the same time, however, they remain virulent for other laboratory animals (white mice).

The mycobacterial catalase content is assessed by the amount of hydrogen peroxide necessary to decompose 10 mg of bacteria (in permanganate titration) within an hour. The ratio between the decomposed catalase peroxide and the total peroxide added to the culture (expressed in per cent), is an index of the given strain's catalase activity.

BLOOD TESTS

Blood Composition

At one time secondary hypochromic anemia was thought to be typical of tuberculosis, often accompanying its pulmonary localisation. In recent years, however, such a view has correctly been discarded as erroneous. Blood changes of the kind mentioned above are observed only at the stage of manifest and mostly irreversible cachexia. It should be borne in mind, however, that secondary

anemia often develops with simultaneous pulmonary, intestinal and renal lesions, particularly in the former. This, probably, may be accounted for by the more manifest disturbance of nutrition in such cases.

Blood Morphology

As regards the hemogram in tuberculosis, relative lymphocytosis has long been noted as symptomatic of the early stage. N. A. Shmelyov's reminder that the hemogram reflects the ability of the marrow to maintain a constant cytological blood content is extremely apt. Hence the significance of repeated tests.

Schilling distinguishes three stages of blood changes in tuberculosis:

1. Neutrophilic—the stage of struggle, when neutrophil leukocytes dominate the blood picture, with a marked regenerative shift to the left; eosinophils are absent, the number of lymphocytes and monocytes reduced;

2. Monocytic, when the disease is being overcome, with an increase in the lymphocyte count; the shift to the left and neutrophil count diminish, and eosinophils appear;

3. Lymphocytic—the stage of recovery with lymphocytosis and neutrophilia and a gradual transition to the normal blood picture.

As regards lymphocytosis, it should be remembered that in a majority of tuberculous patients the phenomenon described in handbooks is extremely rare, and that from the clinical standpoint, the presence of a nuclear shift proper is more important than its degree, though there is an analogy in this respect in post-primary infections. At more advanced ages with clear and progressive processes, the nuclear shift, according to N. A. Shmelyov, reaches 15 to 18 per cent, but occasionally may be absent which is accounted for by inadequate resistance

This shows that the blood changes in tuberculosis may be relied upon and utilised in case of different diagnostic difficulties, as well as for assessment of the course and prognosis. A differentiation difficulty may, however, arise in which the hemogram is likewise of no avail, namely, in miliary tuberculosis, as in enteric, there is leukopenia (lymphopenia) and no eosinophils.

As has been correctly pointed out, monocytosis is frequently found in tuberculous metastasis. Of special interest in tuberculosis, to our mind, is the study of eosinophil leukocytes which are usually sensitive to all kinds of anaphylactic shifts. An example is the eosinophilia observed in bronchial asthma and parasitic diseases, for instance, ascaridosis. The eosinophil leukocytes are extremely sensitive to fluctuations in specific tuberculous intoxication. Observation of fluctuations in absolute counts offers certain additional diagnostic possibilities as regards assessment of the activity of the process. According to the writer's experience the reduction or disappearance of eosinophils in the blood often accompanies exacerbations of the

process, their appearance in the blood and quantitative increase often foreshadowing a remission. If tuberculin were used to provoke such fluctuations in the eosinophil count, there are grounds for supposing that the resultant response would verify the clinical diagnosis.

These considerations form the basis of F. A. Mikhailov's test in which the number of eosinophils in 1 cubic mm of a patient's blood is counted. After that, 0.1 ml of O.T. in dilution No. 9—1:1,000,000,000— is introduced subcutaneously, another eosinophil count being taken after a break of 30 minutes. If, at the second count, the number of eosinophils diminishes by more than 5 per cent, the test is considered to be positive, and if otherwise, negative. The blood is taken from the finger and collected in a melangeur for counting leukocytes, filling it to the first mark, after which Dunger's liquid (1 ml 1 per cent acqueous solution of eosin, 1 ml acetone, 8 ml water) is added up to the second mark. After thorough mixing, the eosinophils are counted in a double Bürker chamber. The result is divided by 18 and multiplied by 100, the product indicating the number of eosinophils in 1 cubic millimetre of blood.

Erythrocyte Sedimentation Reaction

One of the most popular tests is observation of erythrocyte sedimentation (after Fähreus, 1918). It has been noted that the E.S.R. (erythrocyte sedimentation reaction) is considerably higher in inflammation and processes accompanied by tissue disintegration. True, the E.S.R. is also observed to vary in different physiological conditions, e.g., menstruation, pregnancy, and even, to a considerable extent, at different hours of the day, etc.

A higher E.S.R. is noted during inflammatory processes of the most different etiology, e.g., membraneous pneumonia, malignant neoplasm, and so on. It should also be remembered that, on occasions vaccination or such diseases as uncomplicated influenza may likewise bring about an increase in the E.S.R. It must be stressed, therefore, that this test is applied only for prognostic purposes, although in focal lesions an increased E S.R. indicates an active process. When assessed in correlation with all other clinical data, especially serial radiography, the E.S.R. provides a means for more adequate prognosis and control of the clinical evolution of the process.

Usually, there is a certain parallelism between the severity of the tuberculous process and the E.S.R. True, in certain cases of extreme severity accompanied by cachexia the E.S.R. does not increase owing to assimilation disturbances. Satisfactory incapsulation may also be the cause of unaccelerated E.S.R. Cases have been recorded of the E.S.R. being reduced; here repeated counts after one or two hours may be of help. All such cases, however, are exceptional, the rule

being, as already pointed out, a certain parallelism between the severity of the process and the E.S.R.

Basic principle and technique. The nature of the reaction is still under debate. The phenomenon of erythrocyte sedimentation has long attracted the attention of physicians. Even in ancient times much importance was attributed to the so-called *crusta phlogistica.* The results of several studies prompt the hypothesis that the instability of erythrocyte suspension might be caused by an increase in the products of protein disintegration in the blood plasma. The globulin fraction of the serum (fibrinogen + globulin) increases as compared with the serum albumin. Consequently, the erythrocytes gradually lose their negative surface charge due to the absorption of gross dispersed positive proteins. The discharged erythrocytes are agglutinated and the greater the conglomerates of agglutinated blood cells, the more rapidly sedimentation proceeds. The accompanying increase in plasmic viscosity enhances sedimentation.

In the Soviet Union, the E.S.R. is mostly assessed by the Panchenkov technique.

Panchenkov test. Panchenkov's device comprises a tube-holder with 4 pipettes 1 mm in diameter, graduated from 0 to 100. One of the pipettes, previously washed with a 5 per cent solution of sodium citrate, is filled with the same solution to the 50th graduation, and it is subsequently released on to a watch-glass. Blood from the finger is then twice taken by the same pipette until it reaches the upper mark, i.e., 0, it each time being deposited on the watch-glass and mixed with the sodium citrate. The resulting mixture contains blood and sodium citrate in a ratio of 1:4. Then the pipette is filled with citrate blood and put (vertically) in the holder. After 60 minutes the result of sedimentation is noted and recorded as follows: 6-8 mm—norm, 8 to 15 mm—slight increase; 15 to 30 mm—medium increase; over 40 mm—marked increase.

Westergren's method. In this test glass pipettes 3 mm in diameter and 30 mm long are employed A Record-type syringe of 1-2 ml is filled to one fifth of its volume with a 3 to 8 per cent solution of sodium citrate and then used to take blood from a vein The blood mixed with sodium citrate is poured out of the syringe into a cup, thoroughly mixed and sucked up into a pipette up to mark 20 The pipette is then put into a holder, its end having previously been dipped in paraffin and closed with a rubber cap or clamped tube. After leaving it in a vertical position for one or two hours, the number of millimetres of erythrocyte sediment is noted. In healthy males the normal rate is from 2 to 6 mm, and in females from 3 to 8 mm

Electrophoresis

Technique and modifications. In clinical conditions, an estimate of activity in a given case, apart from the E.S.R., may be taken by an essay of the albumin fractions of the blood serum, obtained by electrophoresis on filter paper.

Electrophoresis is the term applied to the movement of colloid particles in an electric field—a process associated with their electrical

charges. The ions of the liquid bear a relatively positive charge, a difference of potentials thus existing between the colloid particle and the surrounding liquid medium which is known as an electrokinetic potential. Different proteins in one and the same liquid may bear different electrokinetic charges, as a result of which the velocity of their movement in an electric field may differ. This phenomenon lies at the basis of the division of protein fractions by the method of electrophoresis. The fundamental principle of electrophoresis on filter paper is that electrophoretic migration takes place on strips of filter paper moistened with a buffer solution and placed between two electrodes, the filter paper being regarded as neutral body. A drop of the serum under test (0.005 to 0.01 ml) is applied to the middle of the paper strip. Electrophoresis is carried out in a buffer solution whose ion power is 0.1 and pH=8.6. The test is made with direct current for a voltage of 120 to 300 V, depending on the time allotted for electrophoresis (4 to 18 hours).

On completing the test, the electrophoregrams are left for 15 minutes in a drying cabinet, where the proteins are fixed by coagulation, after which they are stained with special dyes (bromphenol blue, amido black, etc.). A stained electrophoregram shows vivid spots corresponding to the arrangement of various protein fractions. After staining, the electrophoregram is colorimetrised, the amount of dye bound with the protein serving as an index of the amount of protein in each part of the electrophoregram.

Electrophoresis allows 5 protein fractions in human blood to be distinguished, viz., albumins, α_1-, α_2-, and β- and γ-globulins. In a majority of active cases of pulmonary tuberculosis there is marked hypoalbuminemia. The infiltration and disintegration stages are reflected in the proteinogram by an increase of α_2-globulins, and, in more severe cases, of α_1-globulins as well. In chronic progressive cases there is also an increase of γ-globulins. Quiescence after an infiltrative attack is accompanied by a reduction of α-globulins and later γ-globulins and normalisation of the albumin-globulin factor. In most cases the total blood serum protein does not exceed normal, hypoproteinemia being noted only in the gravest cases, mostly in the terminal period.

Urine

Clinical urine tests must be conducted at every examination. In doubtful cases chemical analysis and sediment study should be accompanied by bacteriological tests.

The presence of tubercle bacilli in the urine indicates a lesion of the kidneys or urinary passageways. The penetration of mycobacteria through a healthy kidney may be considered practically improbable. Very often, tuberculous disorders in the kidneys are accompanied by pyuria. The presence of erythrocytes and renal elements indicates a lesion of the kidneys, the affected side being ascertained

by separate tests of urine catheterised through the ureters from each kidney.

Technique. The centrifuged precipitate is applied to a slide, then dried and fixed. The sample is stained after Spengler or Ziehl-Neelsen and put to microscopy. With a negative result, cultivation after Ghon is advisable, the urine being collected the day before, a sufficient amount of sediment for cultivation being taken.

Feces

In most cases, the presence of mycobacteria in the feces of patients with an active pulmonary process but with no gastrointestinal lesion, merely testifies to swallowing of sputum. A salient feature of tubercle bacilli, it should be remembered, is their resistance to the effects of the digestive juices.

In most cases of intestinal tuberculosis, diagnosis is assisted by the presence of pus and blood in the feces. In such cases examination should be undertaken only after three days of a hemoglobin-free diet.

Technique. The material to be studied is thoroughly mixed in distilled water and centrifuged. The centrifugate is precipitated with an equal volume of 95° alcohol and again centrifuged at high speed for 15 minutes. The sediment is used for preparing smears stained by the usual procedure or for cultivation.

Tuberculin Skin Tests as a Means of Specific Diagnosis

Positive tuberculin tests are evidence of past tuberculous infection and, as a rule, are also obtained in a current tuberculous process. At ages up to two or three a positive tuberculin test indicates an active tuberculous process.

Koch's original tuberculin (O.T.) presents a glycerin extract from a bouillon culture of *Mycobacterium tuberculosis.* Apart from the glycerin extract, i.e., O.T., at present use is made of dry purified tuberculin—the purified protein derivative known as P.P.D. (Linnikova, Zelter). P.P.D. is prepared by ultrafiltration of a tuberculous strain cultivated in a synthetic medium, the filtrate being precipitated by trichloracetic acid and vacuum-frozen.

Tuberculin, even when injected in large doses, evokes no reaction in uninfected animals and man, but if introduced subcutaneously to a child or adult who is ill or has suffered primary infection, it may elicit: (1) a reaction at the site of injection; (2) a general body reaction (high temperature, malaise, etc.), and (3) a focal reaction with increased expectoration and catarrhal manifestations. With lesions in organs other than the lungs, e.g., bone-and-joint tuberculosis, reddening and swelling are noted in the joint, which are sometimes accompanied by the onset or increase of perspiration. At subcutaneous injection of 0.000028 mg of P.P.D., as at injection of 0.01 mg of O.T., more than 90 per cent of all positive tuberculin reactors are revealed without a general reaction.

As mentioned earlier, there are several modifications of the tuberculin test varying in sensitivity. For practical considerations we shall first deal with the *Pirquet skin test.* The original instructions of Pirquet ran as follows: "The skin on the forearm is rubbed with a swab of cotton wool, after which two drops of tuberculin are applied from a dropper or with a glass stick 10 ml apart. Further, a scar is made halfway between the drops with a bore whose platinum tip has previously been heated over a burner. This scar serves as a control, while two others are made with the same instrument in the drops of tuberculin.

The graduated Pirquet test now used comprises the following. Drops of 100, 25, 5, and 1 per cent tuberculin as well as a drop of 0,25 per cent lysol (for control) are applied to the ether-treated skin of the forearm, after which surface scars are made through each drop (from the lowest concentration to the highest) with a bore or scalpel, taking care to avoid bleeding.

After 24 to 48 hours, in positive cases a papule with a hyperemic corolla appears at the site of scarification, while the control shows no sign of reaction. When the Pirquet test proves negative (papule less than 5 mm), the more sensitive *intradermal Mantoux test* is applied.* A short needle is inserted 1 ml below the surface into a skin fold on the shoulder parallel to the skin and 0.1 ml of O.T. in a dilution of 1:10,000 (Mantoux 4) is injected. With negative results, injections are repeated two days later with higher concentrations—up to 1:100 (Mantoux 2). In positive cases, a papule develops at the site of injection. The reaction begins as soon as in 8 hours, taking the form of hyperemia, swelling and, occasionally, vesiculation. After 48 hours the reaction reaches its climax. Temperature reactions and swelling of the regional lymph nodes are extremely rare.

The *subcutaneous tuberculin test* has special aims. Such tests, as an exception, may be employed in non-febrile cases and are contraindicated for patients with cardiac, renal or neurasthenic disorders.

Koch made subcutaneous injections of 0 1-1.5-10 mg of tuberculin Most authors make the first injection with 0.1 mm If no reaction appears, the next dose is administered in not less than 48 hours. If even this evokes no reaction, tuberculosis may be ruled out with a high degree of certainty. The writer employs this test extremely seldom and believes it should be made only by very high-skilled physicians. A positive test, as stated earlier, is followed by a general and focal reaction, and, occasionally, local symptoms Temperature rises of less than 0 5 degrees are ignored, the temperature usually increasing after not less than 10 hours and sometimes even after 1 or 2 days (late reaction).

There is a difference of opinion regarding the frequency of positive subcutaneous tests, yet it no doubt depends on the individual features of the case in hand While some authors have observed a positive reaction in two-thirds of all cases (Romberg), others noted 10 positives out of 120 cases, but these results, too, are approached with caution. Some are sceptical even about clearly positive results. In dispensary practice the subcutaneous skin test, from our point of view, is inadvisable.

* Mantoux' initial proposal was to introduce tuberculin (O T.) intradermally in a dilution of 1:5,000 In the case of negative results, a repeated injection is made with dilutions of 1:1,000 and later 1 100.

Intradermal or subcutaneous tests with 0.1 mg of O.T. may reveal tuberculin sensitivity 100 times lower than displayed by the percutaneous procedure. But the subcutaneous test is seldom used owing to the danger of a focal reaction. According to Hamburger, a positive Pirquet test corresponds to an intradermal sensitivity to 0.01 to 0.001 mg of O.T. As the writer himself has observed, adults react to the Pirquet test in approximately 50 per cent of cases, and in subsequent intradermal tests using from 0.1 to 1 mg of O.T., in up to 98 per cent of cases. Literature on the subject shows that a positive tuberculin test in early childhood indicates an active process.

In recent years it has been found that certain individuals react negatively to tuberculin, but reveal a Koch-type skin reaction to injections of small quantities of B.C.G, the phenomenon being known as *infratuberculin allergy*. In such cases we may also speak of immunity to tuberculosis.

Owing to its simplicity, the *patch test* may be widely employed. A patch of Fresenius plaster is applied to the skin without preliminary ether-treatment. Pin-head particles of tuberculin are arranged in the middle of the patch on a strip of cellophane The plaster is removed after 48 hours, the results being observed 3 to 4 days later when non-specific irritation disappears.

A positive tuberculin test may be obtained even with no clinical manifestations of the disease. Moreover, such a reaction may occur in a currently healthy person who has suffered primary infection many years ago, perhaps even in childhood, the disease having escaped the notice of commensates. But the nearer to early childhood, particularly infancy, the greater the diagnostic importance of a positive skin test. When an unweaned infant proves Pirquet-positive, the extremely short time liable to have elapsed since invasion should be borne in mind. In some cases an experienced pediatrist will easily notice undoubted symptoms of a local lesion, e.g., in the lungs (radiologically).

The older the child, the less diagnostic importance may be attached to the Pirquet test. In older children, as in adults, if clinical findings are absent, it is merely indicative of infection, but not, in itself, of disease. From 14 to 15 years of age, the incidence of infection reaches approximately 30 to 40 per cent, while in infants up to one year old it ranges from 0 to 3 per cent.

In studying infectivity one should bear in mind the possibility of post-vaccination allergy, which also produces a positive tuberculin reaction.

In infants and older children the appearance of a positive tuberculin reaction marks the onset of the so-called *allergic period*, which preceded by the pre-allergic stage, continuing for an average of 3 to 8 weeks.

This period, apparently, may be regarded as the incubation period of tuberculosis. Its duration is considered inversely proportional to the number of invading mycobacteria. In this stage the mycobacte-

ria disseminated through the body do not reveal their presence by an obvious signs. This is followed by the stage of the primary pneumo glandular complex mentioned above, accompanied by allergi changes clinically demonstrable by tuberculin skin tests.

As stated earlier, Pirquet-positives may occur among both health and sick individuals.

Special significance is attached to the moment of tuberculi conversion, i.e., the period when an earlier negative tuberculin reacto begins to react positively. Physicians think that the period o conversion deserves greater attention from the standpoint of antitube culosis prophylaxis as far as children and adults are concerne Depending on their general condition, individuals in whom tube culin conversion has been discovered require special care in the forr of adequate physical exercise and, in certain cases, general suppo tive measures of a hygienic and dietary nature, or, in other case chemoprophylactic treatment with INH.

In some cases tuberculin conversion indicates the onset of tube culosis, which may be illustrated by the following instance.

Patient O.N., female, age 15. No tuberculosis in the family. Tuberculin test repeatedly negative (last test January 1, 1948).

Disease began April 13, 1948, with sharply manifest temperature fluctuation (37.1 to 39°C), anorexia, lassitude, emaciation. Blood: Hb 58 per cent, er. 3,500,00 leuc. 10.000, eos, 1 per cent, band cells 15.5 per cent, segmented cells 51 per cen lymph. 28 per cent, mon. 4 5 per cent, E.S.R. 60 mm per hour. Symptoms of a loc pulmonary lesion (cough, catarrh) absent. Clinical picture accompanied by vivid manifest tuberculin reaction (Pirquet) with necrotic papule (Fig. 31). Lung radi graph (April 20, 1948) showed two foci at the right-pulmonary and glandula (primary complex, bipolar stage).

This does not exhaust the practical importance of the tuberculi test. It should be remembered that the intensity of the Pirquet reac tion may vary broadly—from totally negative with marked cachexi in severe cases to acutely manifest, as in certain other forms especially in the primary period of infection. Here the graduate tuberculin skin test may assist in evaluating the activity of the process

Negative anergy may be observed as a transient phenomeno following diseases like measles, influenza, etc., an exception bein cachectic cases in which there is a fatal excess of toxic substance associated with the severity of the process. In the latter it serve merely to confirm impending paralysis of the defensive powers wit all the ensuing consequences. In such cases therapy is usuall powerless, and, as will be further evident, the use of tuberculin fo therapeutic aims is strictly contraindicated for Pirquet-negatives since the body is already supercharged with tuberculin, whic renders its repeated administration senseless.

Positive anergy may sometimes be noted instead of normergy i as yet uninfected individuals. According to some authors, it devel ops during hyperimmunity, when tuberculin introduced into th body is destroyed without any noticeable clinical reaction.

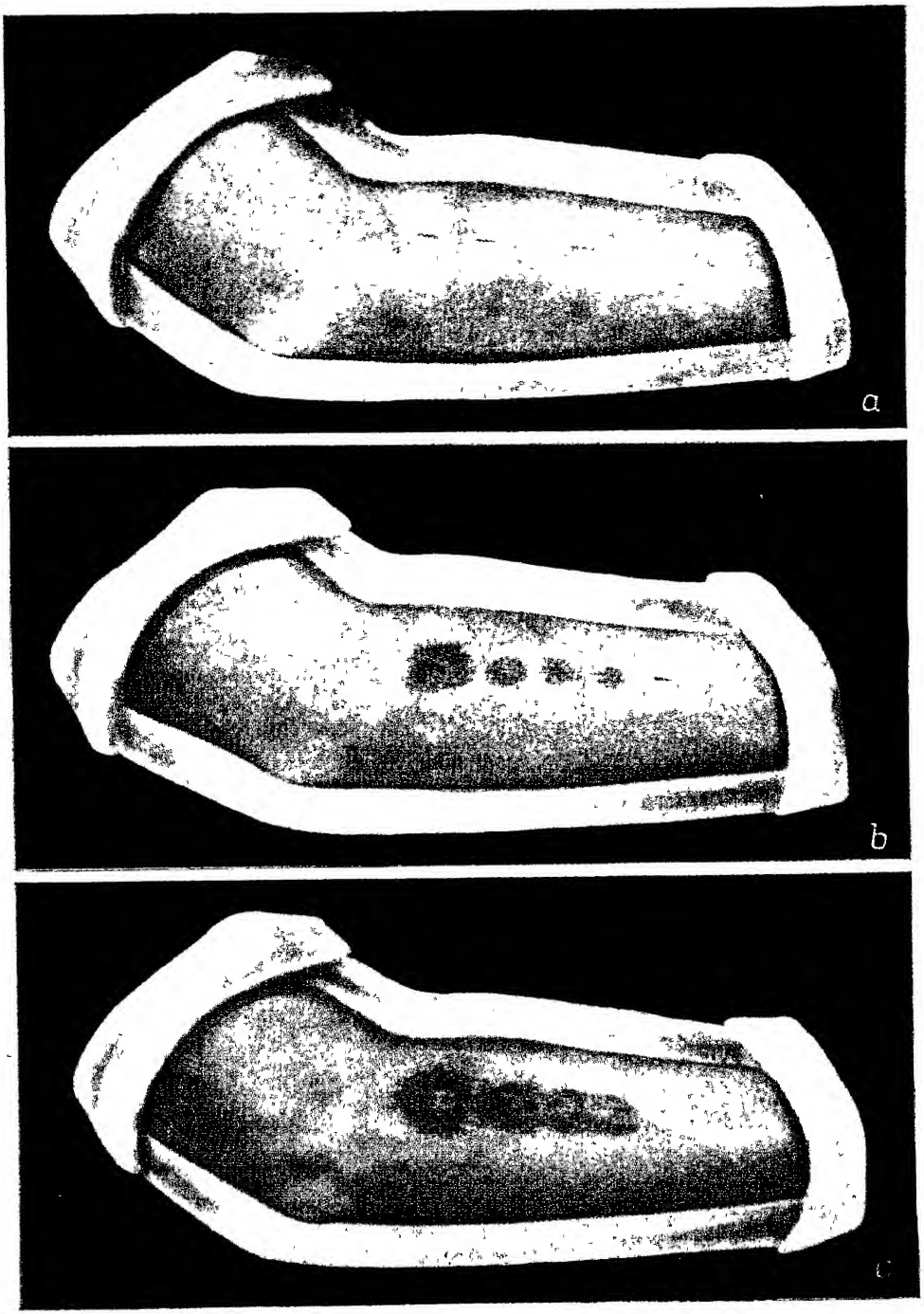


Fig. 31. Graduated tuberculin test
(a) negative; *(b)* moderately manifest, *(c)* acutely manifest

CHAPTER VI

CLINICO-ANATOMICAL CLASSIFICATION OF TUBERCULOSIS

The clinical classification of tuberculosis which has been adopted in the U.S.S.R. is founded on extensive morphological research and confrontation of morphological findings with clinical pictures of the disease at different stages of the process. A major part in building up the acting nomenclature was played by comparative analysis of radiological and anatomical findings, i.e., parallel study of radiographs and pathoanatomical preparations. This proved especially important in establishing the relationship between different pictures, both in the process of evolution, i.e., progression, and in the course of reverse development (involution) and healing. In the classification adopted at the 5th Congress of Soviet phthisiologists in 1948,* much attention is given to pulmonary tuberculosis as one of the most frequent localisations, having special clinical and epidemiological importance. Extrapulmonary localisations, however, are also sufficiently well represented.

The current classification will, of course, be modified as new data come to light, but the basic differentiation between the clinical forms of tuberculosis will no doubt remain.

This system of classification enumerates the clinical forms of the disease together with an outline of the course in its different stages (infiltrate, disintegration, resorption, consolidation, noting the coverage of the lung fields, the degree of compensation (total—A, subcompensation—B, decompensation—C) and, of course, bacillarity.

Compensation implies the return to normal of all physiological functions as well as the temperature and blood picture. In subcompensation, the patient shows subfebrile temperature fluctuations, lassitude, malaise, increased E.S.R., and a toxic neutrophil shift to the left, all indices being moderately manifest. Under decompensation we presume a febrile syndrome with increased temperature, sweating, anorexia and emaciation.

* The first variant was drawn up by Prof. A. Y. Sternberg and adopted by the 2nd All-Union Antituberculosis Congress in 1922.

These phenomena are all formulated in the following table which, despite the evident need for addenda and amendments, has played a major part in the systematisation of early casefinding and dispensary follow-up, and has remained in use to this day.

A. PULMONARY

Forms

1. Primary complex.
2. Tuberculosis of the bronchial glands.
3. Acute miliary tuberculosis.
4. Subacute and chronic pulmonary tuberculosis with hematogenous dissemination.
5. Focal pulmonary tuberculosis.
6. Infiltrative pulmonary tuberculosis.
7. Caseous pneumonia.
8. Chronic fibrocavernia.
9. Pulmonary cirrhosis.
10. Pleuritis.

Course

1. Stages of evolution: (a) infiltrative; (b) disintegration, dissemination; (c) resorption; (d) consolidation, calcification.
2. Spread and localisation by lung fields, in each lung separately (1, 2, 3—recorded in the form of fractions).
3. Degree of compensation: (a) compensated—A; (b) subcompensated—B; (c) decompensated—C.
4. Bacillarity: BK+, BK—, BK± (periodic).
5. Presence of elastic fibres—E.F.+; E.F.—

B. EXTRAPULMONARY

Forms

1. Tuberculosis of the bones and joints.
2. Tuberculosis of the peripheral glands.
3. Skin tuberculosis.
4. Tuberculosis of the serous membranes (pericarditis, peritonitis, polyserositis).
5. Tuberculous meningitis.
6. Tuberculous laryngitis.
7. Intestinal tuberculosis.
8. Urogenital tuberculosis.
9. Tuberculosis of other organs.

The necessity of augmenting and modifying the cited classification may be demonstrated briefly by the following considerations. On the one hand, the use of the most up-to-date methods of examination, particularly bronchography and tomography, has led to deeper knowledge of the localisation and dynamics of tuberculous organic changes. On the other, the assessment of functional changes associated with tuberculous infection has become more perfect. The present-day concept of the segmental structure of the lungs and the development of pathoanatomical concepts of the onset and evolution of tuberculosis and some of its forms, e.g., initial manifestations, tuberculomata, etc., are of necessity borne in mind in clinical practice.

With the extensive contemporary use of pulmonary surgery and considerably greater frequency of recovery and the establishment of indications for intervention necessitating a much more precise definition of lesions in regard to localisation and focal features, the modern concept of the segmental structure of the lungs becomes especially important. Most essential in this respect is the structure of the bronchial tree and tracheobronchial ramifications. It has been established that each of the pulmonary segments has its own draining bronchus. According to the universally adopted international nomenclature, each lung is divided into 10 segments corresponding to the 10 segmental bronchi.

Segmental bronchi of the right lung		Segmental bronchi of the left lung	
Superior lobe.	apical, posterior, anterior.	Superior lobe.	apical, posterior, anterior
Median lobe	lateral, medial.	Lingula:	superior, inferior.
Basal lobe.	superior, basal medial, basal anterior, basal lateral, basal posterior.	Basal lobe:	superior, basal medial, basal anterior, basal lateral, basal posterior

Fig. 32 shows a diagram of the distribution of segmental bronchi with a model of the pulmonary segmentation.

Each segment is furnished with a bronchus of the first order, a corresponding branch of the *a. pulmonalis*, two veins and an intrasegmental nervous system. On account of its structure, each segment may, to a certain degree, be regarded as an autonomous functional unit. In surgical intervention (segment resection) the segments are separated by the blunt technique along the intrasegmental veins.

However, the idea of the importance of the segmental structure of the lungs is confirmed not only by surgical practice. Apparently the evolution of the process, in particular its bronchogenic spread, is likewise somehow associated with the segmental structure of the lungs. In this respect there is an acute need for further pathoanatomical and experimental research on a number of clinically important points.

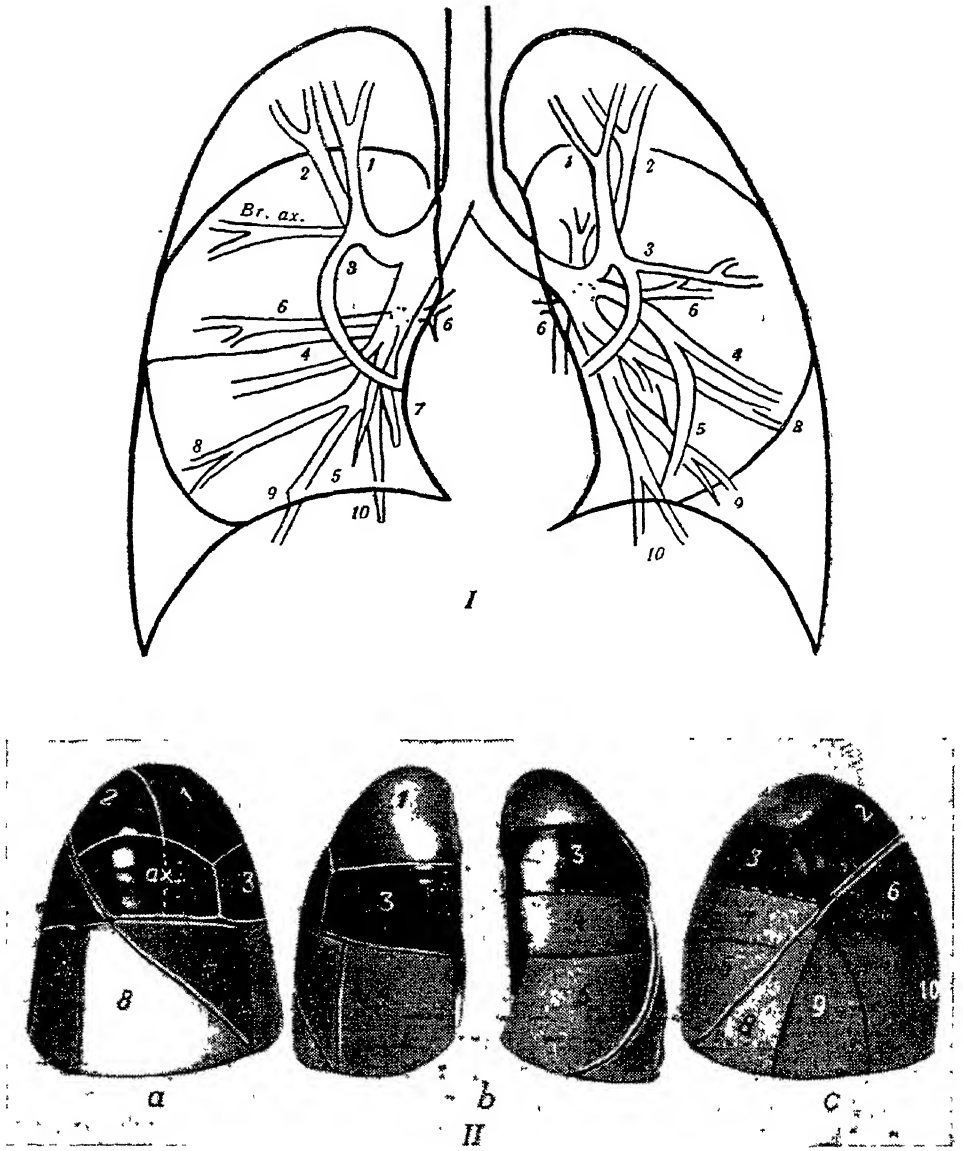


Fig. 32. Distribution of segmental bronchi *(I)* and model of pulmonary segments *(II)* after Kovacs and Žebek.

Left–right lung, right–left lung; *a* and *c*–side view of the lung, *b*–front view of the lung. Figures denote numbers in order of segmental bronchi and pulmonary segments, *ax*–impermanent axillary segment, *Br ax–Bronchus axillaris*

The practical use of the described classification of tuberculosis will be illustrated further by clinical examples chosen in accordance with the basic forms of tuberculosis of the lungs and other organs.

CHAPTER VII

CLINICAL FORMS OF PULMONARY TUBERCULOSIS

CLINICAL FORMS OF PRIMARY TUBERCULOSIS

For practical purposes of rational prophylaxis it is essential to know how and when the disease begins. The first object is, of course, to establish the incidence of primary infection. The answer to this question is furnished by positive reactions to the Pirquet tuberculin skin test and, if that should prove negative, by the Mantoux intradermal test.

As mentioned earlier, primary tuberculous infection is mostly observed in childhood. Positive tuberculin reactions in infancy (up to 3 or 4 years of age) often indicate disease. At older ages a positive reaction mostly bespeaks an earlier infection, but not necessarily current disease which particularly refers to adolescents and adults. A sharp ("rich") skin reaction to lower tuberculin dilutions should warn the physician against the possibility of an active process, calling for comprehensive examination of the particular case.

Recent research has demonstrated a gradual shift of primary infection towards later age groups. This, of course, is an outcome of the entire system of prevention and specific therapy.

Previous chapters and the data cited have shown how many forms primary tuberculosis may take. As mentioned in the subchapter on the morphology of primary tuberculosis, a typical feature of such conditions is the clear involvement of the lymphatic system and massive caseous necrosis of the lymph nodes. For practical purposes, the following basic forms should be distinguished:

1. Primary tuberculous complex;
2. Tuberculous toxicemia (postinfectional, early and remote), associated with tuberculous changes in the lymphatic system, in particular with tuberculosis of the intrathoracic lymph nodes;
3. Pneumoglandular forms, frequently involving the serous membranes, the pleura in particular.

Any of these pictures, especially that of the primary complex, may be accompanied by the tuberculo-allergic symptoms previously

described, viz., (a) cutaneous *erythema nodosum*; (b) phlyctenulous conjunctivitis; (c) extrapulmonary tuberculous metastases.

These symptoms signify a drastic increase of sensitivity and a tendency towards hematogenous metastasis.

Primary Complex

In a number of cases the only apparent symptom of primary tuberculosis may be a positive tuberculin reaction, especially tuberculin conversion, i.e., the emergence of a positive reaction, instead of the earlier observed negative response.

Occasionally, only the radiographical discovery of a characteristic calcified focus in the lung and similar petrificates in the hilar zone indicate an earlier primary tuberculous complex. On the other hand, there are cases when symptoms of influenza or pneumonia with temperatures of up 39° C camouflage a marked pulmonary lesion, often with random interscapular small-sized rales on the background of harsh breathing. In such cases, the lung X-ray reveals a more or less widespread density of the perifocal inflammation type, mostly in the hilar zone, and usually in one lung. With the involution of the changes, two poles are revealed—pulmonary (an incipient Ghon focus) and glandular. Subsequently, only scattered traces may remain of a consolidated primary complex.

Patient F. K., age 8, schoolboy. Parents never had tuberculosis In early childhood had measles, whooping-cough, scarlet fever, chicken pox, once—at the age of 18 months—pneumonia After quinsey suffered in October 1947, temperatures up to 39° persisted for 2 weeks accompanied by lassitude, anorexia, emaciation. No cough or expectoration evident At the same time became Pirquet-positive. Harsh breathing in the medial segment of the right lung, catarrhal phenomena absent. Radioscopy revealed a fresh primary complex in the medial segment of the right lung with perifocal inflammation (Fig 33, *a*).

Sanatorium treatment brought improvement of general well-being, with resorption of the perifocal inflammatory changes in the right lung During $1^1/_2$ years' follow-up the perifocal inflammation around the regional lymph nodes disappeared, followed by induration of the pulmonary focus (Fig. 33, *b*).

Conclusion a case of primary complex with a benign course; involution due to hygienic, dietary and climatic treatment without antibacterial therapy.

Tuberculous Intoxication

Many childhood diseases are observed to be accompanied by general functional disorders.

Soviet workers have established that these disorders (anorexia, dyspepsia, nervous hypersensitivity, subfebrile, usually irregular temperature) are often conditioned by tuberculous intoxication. The observations of A. A. Kissel, who gave vivid clinical pictures of such children, are especially instructive (A. A. Kissel's syndrome).

As Kissel correctly comments, the basic localisation at this stage is the lymphatic system, in particular the intrathoracic and periph-

eral lymph nodes. The latter are easily detected by palpation along the sternocleidomastoids, while tuberculous lymph nodes of the mediastinum which are seldom detectable by physical methods, often appear on dorso-ventral and especially profile radiographs. However, the clinical picture does not always exhibit hypertrophic intrathoracic lymph nodes demonstrable by modern examination techniques. If they are absent, the syndrome of tuberculous intoxication predominates along with a markedly positive tuberculin skin test.

Recent works have brought to light a variety of general functional disturbances occurring at the stage of invasion (early generalisation) in which, according to Z. A. Lebedeva, A. I. Kudryavtseva and E. Z. Sorkina, dissemination sets in even before the emergence of a primary complex.

We can distinguish mild and severe forms of tuberculous intoxication, early and chronic. Occasionally, apart from general functional disturbances, marked tuberculo-allergic symptoms are noted in the form of *erythema nodosum* or phlyctenulous conjunctivitis.

Recently, the writer observed such a picture in a pale and wasted 12-year-old girl Marked emaciation, secondary anemia with reduced hemoglobin were accompanied by moderate dilatation of the hiluses, enlarged cervical lymph nodes and diffuse *erythema nodosum.* At emergence of the latter, the temperature rose to 39°C. General supportive measures and chemotherapy led to rapid improvement in the general condition.

Tuberculous Bronchadenitis

As mentioned earlier, tuberculous changes in the hilar and mediastinal lymph nodes may continue to develop after the primary complex has subsided and even calcified. Occasionally such a course is observed after more or less marked remission. Here we have to do with a special phenomenon which Soviet specialists (A. I. Kagramanov) call latent microbism. Essentially, it is based on the ability of mycobacteria to prolonged survival within an organ, especially a lymph node, in a dormant state which, however, may be interrupted when under malignant changes of body reaction they begin multiplying and cause progressive inflammatory lesions. The process may involve various glandular groups, e.g., *lgl. tracheales dextrae et sinistrae, lgl. tracheobronchialis dextrae et sinistrae, lgl. tracheobronchialis inferior, lgl. bronchopulmonales.*

Lesions of the hilar nodes, likewise known as interlobar, since only an extremely fine layer of the parenchyma separates them from the interlobar pleura, are often accompanied by involvement of the latter. In some of these lesions we have to deal with the continuing development, initially latent, of a tuberculous lymphadenitis, originally part of the primary complex, in others with an exacerbation of quiescent lesions with intra- or periglandular inflammation. In a number of instances the lymph nodes are beset by massive caseation

which mostly occurs in childhood, but may likewise be observed in adolescence and, comparatively seldom, in adulthood.

Radiographically, we distinguish: (1) tumour-like tuberculosis of the intrathoracic lymph nodes; (2) non-tumour-like forms of nodal lesions. On a number of occasions perifocal infiltrative changes develop around the affected glands. The process may involve the interlobar pleura (interlobar pleurisy).

The diagnosis of *tumour-like* forms usually presents no difficulties (Fig. 28), but in some cases requires comprehensive examination, envisaging the possibility of other systemic diseases, primarily lymphogranulomatosis and malignant neoplasmata.

At some stages tuberculous changes are accompanied by high temperature, occasionally irregularly subfebrile, with a high E.S.R. and all the described symptoms of tuberculous intoxication as well as a markedly positive tuberculin skin test. In a number of cases the lymph node clusters are so large that they constrict the bronchial passageways and stimulate coughing, which is especially manifest in lesions of the lymph nodes in the region of the tracheal bifurcation. In other cases atelectasis develops due to extreme constriction of the lumen of the draining bronchus, involving segments or entire lobes. Thus, for example, there are descriptions of a characteristic triangular shadow in atelectasis of the medial lobe of the right lung. In atelectasis of the superior lobe of the same lung radiography reveals a massive density in the lobar area with a clear-cut superiorly convex shadow boundary, high diaphragmic cupola and mediastinal displacement to the right. Pathoanatomically the dilated lymph nodes resemble cooked chestnuts or potatoes.

There are also bilateral lesions of the lymph nodes, which are especially often observed in childhood. On certain occasions the tuberculous process spreads from the caseous lymph node to the adjoining bronchus (Fig. 34), giving rise to bronchoperforations, the so-called bronchofistulous forms which were known to Laennec and described by A. I. Abrikosov. The process is often accompanied by metastasis and specific infiltration of the pneumoparenchyma, or caseous bronchopneumonia. Bronchoscopically pictures of infiltrations of the bronchial wall with fistulation are highly informative.

Non-tumour-like tuberculous lesions of the intrathoracic lymph nodes, associated with intraglandular growth of specific granulation tissue, may proceed latently, with moderate symptoms of tuberculous intoxication, anorexia, fatigue, and a tendency to chills.

Chronic Primary Tuberculosis

Primary tuberculosis is not as frequently encountered in adults as in children. In wartime, however, due to generally reduced resistance, adults with clinical pictures of primary tuberculosis were often observed. In addition, it is important to note another possible

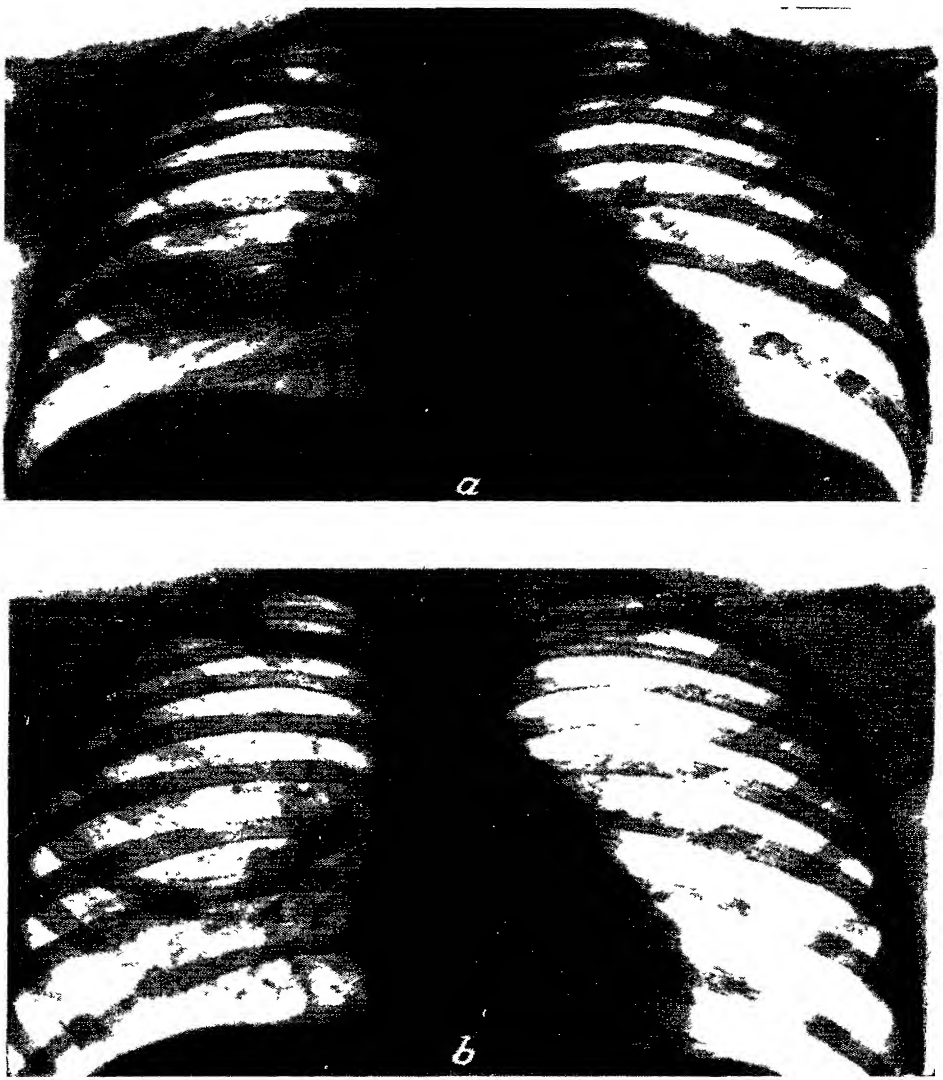


Fig. 33. X-rays of patient F K
(a) before treatment, primary tuberculous complex in right lung, *(b)* after hygienic and dietary treatment in sanatorium

Fig. 34 Tuberculosis of lymph nodes and lesion of bronchial walls

line of development of the disease. Having resulted directly from a primary infection, for many subsequent years and even decades it may run a wave-like course with prolonged and sometimes perennial remissions, becoming a chronic process. The morphology of such conditions was placed by the Soviet pathologist V. T. Shwaitsar under chronic primary tuberculosis. Such pictures are familiar to any experienced physician. The above may be illustrated by the following example.

Patient N. N., at the age of 17 (1907), after prolonged family contact with a tuberculous relative, revealed unmotivated periodic gastrointestinal dyspeptic disturbances. In 1911, after repeated attacks, he had an operation for acute appendicitis. The dyspeptic disorders, however, continued. In 1912, at the age of 22, he suffered hemoptysis with no marked changes in the lungs which was confirmed physically and radiologically. Occasionally he had short spells of subfebrile temperature (37.3 to 37.5°C). In June 1913, after intense mental exertion, he had two severe pulmonary hemorrhages, revealing hilus-catarrh on the left side and a small perihilar density in the left lung The Pirquet test was positive, the sputum twice proving to contain *Myco. tuberculosis.* The patient spent 6 months in a sanatorium.

In 1914, he expectorated small caseous necrotic particles with tubercle bacilli. Later, a return to good health with complete occupational rehabilitation, stable cessation of bacillarity and residual sclerotic changes in the perihilar zone of the left lung was stated. Blood without pathological changes. From 1915 to 1950 the picture was that of recovery from primary hilar, probably bronchofistulous, tuberculosis (by the modern nomenclature). When coughing, random small-sized (sclerotic) rales were detected stethacoustically in the perihilar zone of the left lung

In 1950, after excessive work, pneumonia masked as an influenzal syndrome developed at the same site, with temperature of up to 38°C and subsequent pulmonary hemorrhage, indicating classical relapse. After the administration of 60 g of streptomycin, the pneumonic changes were almost totally resolved with residual sclerosis. In 1951, pneumonic infiltration reappeared at the same site with as yet almost indeterminable destruction. Two and a half months in a sanatorium with streptomycin (67 g) resulted in complete rehabilitation with resorption of the perifocal inflammation. Bacillarity ceased. In 1952-59 there was every indication of clinical recovery. Sclerosis in the interclaviculohilar area was more pronounced, with concomitant bronchiectases.

Such cases, occasionally observed in adults, are adequately explained in the pathoanatomical studies of V. T. Shwaitsar, A. I. Strukov and K. A. Deli. The evolution of the disease is clearly associated here with the primary changes in the lungs and intrathoracic lymph nodes with quite typical perihilar localisation.

Diagnosis. As mentioned earlier, the described changes in the intrathoracic lymph nodes are observed along with a positive tuberculin reaction. The procedure mostly in use is the graduated Pirquet skin test. Percussion of the interscapular area may produce positive results with large clusters of tuberculous bronchial lymph nodes, but this seldom occurs. The author has repeatedly witnessed a flat sound in cases of a lesion of the paratracheal lymph nodes in the first intercostal space at the left with perifocal inflammation of the pneumoparenchyma; during a slight cough small-sized moist rales may be heard posteriorly, around the hilus. Ocassionally stethoscopy may reveal pleural friction sounds.

Owing to the development of thoracic radiology direct percussion of the bony spinal processes after Koranyi or auscultation of murmurs and bronchophony after D'Espine are now seldom employed.

Radiological studies should include: (1) radioscopy (multiaxial, after Prozorov); (2) dorso-ventral lung radiography; (3) profile radiography.

Profile radiography offers a view of the posterior mediastinal area, thus giving visual access to glandular clusters which in dorso-ventral radiography are obscured by the shadow of the heart (Fig. 28).

In addition, profile radiography often reveals densities typical of interlobar pleurisy which are not always clearly demarcated in conventional radiography.

Conventional radiography gives a fairly good view of periglandular inflammation in the pneumoparenchyma, which resorbs quite rapidly under adequate general treatment and chemotherapy.

One must mention yet another radiological picture often appearing in tuberculosis of the bronchial lymph nodes, when strand-like adhesions, regarded as lymphangoitis and later as perivascular lymphangoitic scleroses, extend from the hilus to the periphery, especially in the interclaviculohilar area. We have often observed infiltrations superimposed, subsequently, on such lymphogenous conditions (Shtefko).

Differential diagnosis is least difficult in children and in cases when the disease is accompanied by the characteristic intoxication syndrome with positive tuberculin reactions. Here there is a possibility of lymphogranulomatosis in which the peripheral lymph nodes are likewise usually involved. Perihilar pneumocarcinoma should also be considered in differentiating adult cases. It is mostly observed in males and, depending on the extent of mediastinal lymphoglandular involvement, is accompanied by pain and dyspnea.

It should also be remembered that hilar thickening may occur in pneumoconiosis. Nor should one overlook Boeck's sarcoidosis which is also accompanied by hilar thickening (See chap. IX, Diagnosis of Pulmonary Tuberculosis), likewise observed in congestion of the lesser circuit.

Therapy comprises chiefly dietary and hygienic measures. In pronounced stages of the disease, sanatorium treatment is prescribed with continuous combined chemotherapy (phthivazid and P.A.S.).

HEMATOGENOUS DISSEMINATION

Pictures of hematogenous dissemination are among the most common in both acute and chronic forms of tuberculosis. The clinical symptoms may range from limited eruptions in any particular area of a lung to conditions involving both lungs, and from chronic forms to acute general miliary tuberculosis.

The source of dissemination may be a tuberculous, particularly caseous focus anywhere in the body (See diagram, p. 100). The bacilli are quite frequently borne out with the lymph flow from softening caseous matter in unhealed foci within the glands involved in a primary complex, travelling, for instance, via the thoracic duct and venous sinus into the right heart. In this way, isolated dissemination may occur in the lesser circuit, i.e., the lungs. When large numbers of mycobacteria erode into the vessels, some of them may travel through the wide pulmonary capillaries into the larger circuit, and when eroding directly into the pulmonary veins, straight into the left heart and thence into the peripheral vessels of the larger circuit, causing lesions of various organs.

The possibility of periodic replenishment of mycobacteria in the blood is an established fact. In pulmonary tuberculosis, Loewenstein was able to isolate mycobacteria from the blood in 38.5 per cent of all cases by cultivation in special media. This figure is, of course, unduly high, but, nevertheless, the fact that tubercle bacilli may pass into the blood has been definitely confirmed. It should be remembered, however, that mere bacillemia is not enough to give rise to disseminated tuberculosis. Apart from massive invasion, its emergence depends on special circumstances, viz., reduced resistance, which becomes clear in the light of what was said earlier about allergy being accompanied by marked hypersensitation.

Pathoanatomists believe that 30 to 40 per cent of all progressive tuberculous lesions are hematogenous. For a physician, an irrefutable confirmation of hematogenous origin is the presence of diffuse foci in the lungs and occasional extrapulmonary metastases, e.g., lesions of the eyes, *erythema nodosum,* lesions of the bones and joints, kidneys, etc. Hematogenous dissemination may now be stated with considerable certainty on the basis of a well-read radiograph, provided there is bilateral involvement.

The diagram given further outlines the development of hematogenous dissemination in the larger and lesser circuits, corresponding to the various forms of the condition which are as follows:

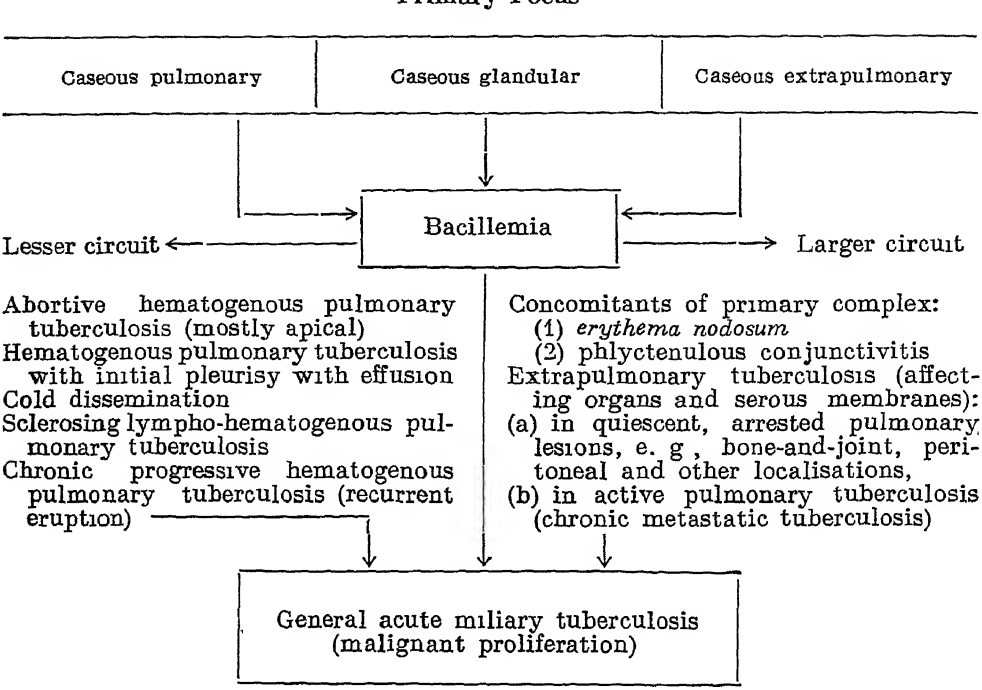
1. Acute general miliary tuberculosis, constituting a separate clinical case;

2. Chronic hematogenous disseminated tuberculosis of limited spread either evolving from a single eruption or developing with repeated metastases in both the lesser and larger circuits (pulmonary and extrapulmonary respectively).

Not infrequently such forms begin with a serous pleurisy with effusion or are accompanied by pleurisy as they develop;

3. In a number of cases radiography demonstrates small diffuse petrifactions, whose emergence might have been continuously preceded by vegetative symptoms: lassitude, fatigue, occasional insomnia, tachycardia, etc. The temperature either does not rise at all or

HEMATOGENOUS TUBERCULOSIS



reaches subfebrile levels. As has been noted earlier, in a definite percentage of cases such foci may be a source of reactivation, initiating progression.

Acute Miliary Tuberculosis

A classic expression of hematogenous dissemination in both primary and secondary infection, as stated in the chapter on pathological anatomy, is general acute miliary tuberculosis, whose course resembles that of an acute septic condition. The disease is mostly observed in childhood and adolescence.

Remittent high fever with temperatures of up to 39 and 40°C and more, mounting dyspnea and cyanosis, indicates predominantly pulmonary involvement. However, the minimal productive tubercles not only spread through the lungs, but invade different organs, including the meninges. In cases of vital lesions of the meninges, the clinical picture is dominated by the syndrome of tuberculous meningitis. The number of tubercles in different organs may vary, their size

ranging from that of a millet grain to that of a lentil. In the lungs the tubercles are distributed evenly, their size gradually diminishing in the craniocaudal direction. The apical segments are almost invariably involved, as opposed to focal spread in carcinoma, pneumoconiosis, etc.

Clinically, we distinguish: (1) the typhoid (septic) form; (2) the form with meningeal localisation; (3) the predominantly pulmonary form.

The onset is often abrupt, occasionally after a period of malaise, accompanied by high fever, profuse sweats, rapidly mounting dyspnea and tachycardia, as opposed to the bradycardia observed in enteric. Consciousness is often affected. In the early stages physical and radiological examination (radiography is mandatory) may show no pathology in the lungs. But subsequently the pulmonary percussion sound acquires a tympanic quality due to accompanying emphysematous changes, localised small-sized moist rales possibly being audible at closely adjacent sites. A well-read radiograph at this stage reveals a more or less abundant spread of fine foci. The X-ray picture occasionally resembles a snowstorm. At this stage there are irrepressible mounting dyspnea and cyanosis.

The blood picture shows leukopenia, particularly lymphopenia, which is linked with grave intoxication, and eosinopenia. The diazo reaction is negative. In 75 per cent of all cases, eye-ground examination shows greyish-white and yellowish-white circular or elongate spots with hazy contours. These are the tubercles in the choroid. Due to an excess of toxic substances, the tuberculin test may be negative. The spleen is enlarged.

Diagnosis is based on confrontation of the severe general condition, high fever, dyspnea and cyanosis with the characteristic picture of tuberculous dissemination in the lungs revealed by radiography. The presence of an earlier known focus, e.g., in the intrathoracic lymph nodes and lingula, confirms the diagnosis.

Differential diagnosis should envisage enteric, but a positive Vidal test and the absence of marked changes such as dyspnea and cyanosis in the respiratory and circulatory organs, as well as the presence of bradycardia, confirm enteric, of which bradycardia is so typical. In carcinosis the chief symptom is dyspnea, mostly without high fever.

The meningeal syndrome is a frequent concomitant of acute miliary tuberculosis.

Treatment. Under combined chemotherapy the clinical picture alters drastically in the course of several days. The principal drugs used are streptomycin, phthivazid and P.A.S. Recovery in this disease, only ten years ago considered lethal, is now guaranteed if prompt diagnosis and vigorous treatment is undertaken. The following clinical observation may serve as an example.

Patient T., female, age 20. In May 1951 evinced lassitude, fatigue, coughing, expectoration, night sweats, emaciation. Contact with tuberculous patients denied. Radioscopy instituted at the time showed no pathological changes in the lung fields.

Heart with smooth waist. General condition continued deteriorating On June 15, 1951, temperature rose to 39.5°C accompanied by acute weakness and dyspnea. Diagnosis: miliary pulmonary tuberculosis, exudative pericarditis, for which the patient was hospitalised, June 23.

General condition on admission grave: temperature up to 40°, skin pallor, cachexia, cyanosis of the mucosa, acrocyanosis, dyspnea (36 aspirations per minute). Heart boundaries distended bilaterally, heart diameter 20 cm. Murmurs dull. In both lungs harshness accompanied by multitudinous moist small-sized rales and diffuse dry rales. Sputum contained *Myco. tuberculosis* and elastic fibres. Blood. Hb 52 per cent, leuk. 8,500, band cells 7 per cent, segmented cells 68 per cent, lymph. 20 per cent, mon. 5 per cent, E.S.R. 46 mm per hour. Radiography, June 23: heart enlarged in all dimensions, shadow clear-cut, diameter 18 cm. Mediastinal shadow bottle-shaped, typical of exudative pericarditis, both lung fields evenly mottled with pin-head tubercles (Fig. 35).

Directly on admission began receiving streptomycin intramuscularly in a dosage of 0.5 g twice a day. Oxygen therapy applied as well. On the 10th day revealed the meningeal syndrome. Spinal puncture confirmed the diagnosed tuberculous meningitis (protein 0.03 per cent, cytosis 118 in 1 cubic mm, Pandy's test +++, sugar 31 mg%). On the next day treatment was augmented by suboccipital injection of streptomycin. Simultaneously P.A.S. was given in a dosage of 6 g daily. Despite the onset of basilar meningitis, improvement was noted in the heart and lungs.

The clinical course took altogether 10 months during which the patient received 125 g of streptomycin intramuscularly, 65 suboccipital injections of streptomycin in doses of 50,000 u, 1,600 g P.A.S. General condition after treatment quite satisfactory. Pulmonary foci completely resolved (Fig. 36)

On discharge, no deviations from the normal were observed in the nervous, respiratory or circulatory systems.

During two years' follow-up the patient has remained well and able to work

Conclusion: military pulmonary tuberculosis, pericarditis and tuberculous meningitis cured as a result of prolonged antibacterial therapy.

Tuberculous Meningitis

Very often the meningeal localisation, mostly basilar, is not immediately revealed. The appearance of pronounced meningeal symptoms is preceded by a prodromic period with malaise—lassitude, anorexia. Later there is an upsurge of agonising headaches accompanied by occipital rigidity (head retraction), Kernig's symptom and drastically exaggerated tendon reflexes. In a number of cases diagnosis is assisted by the presence of general miliary tuberculosis. With involvement of the cranial nerves (*nn. abducens and facialis*), characteristic paralyses develop. If tuberculous meningitis is suspected, diagnostic lumbar puncture is required. In the acute stage of the disease the spinal fluid, currently regarded as a secretion of the nerve cells and a dialysate of the blood plasma, is transparent and slightly opalescent, issuing under high pressure and at prolonged maintenance forming a fibrinous retina, film or web. On many occasions it reveals *Mycobacterium tuberculosis*. Hypoglycorrhachia (sugar reduction) is up to 10 or 13 mg%. Cytosis, i.e., an increase of cellular elements at the expense of lymphocytes, is noted in the spinal fluid.

The following table gives the normal and pathological composition of spinal fluid.

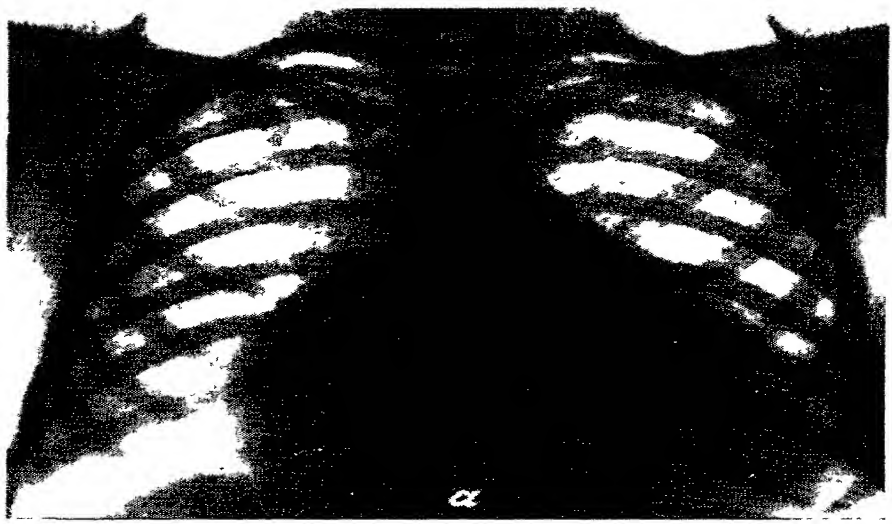


Fig 35. X-rays of patient T Acute miliary tuberculosis, tuberculous meningitis and pericarditis before treatment

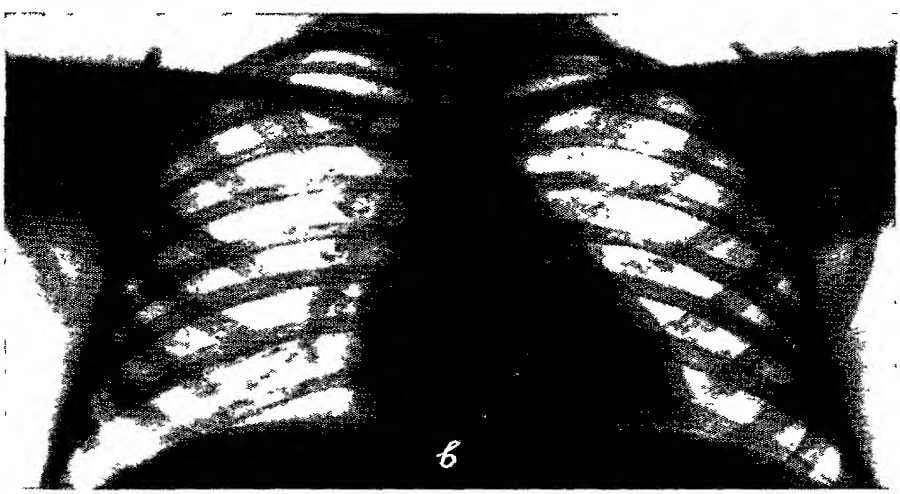


Fig 36 X-rays of the same patient after treatment

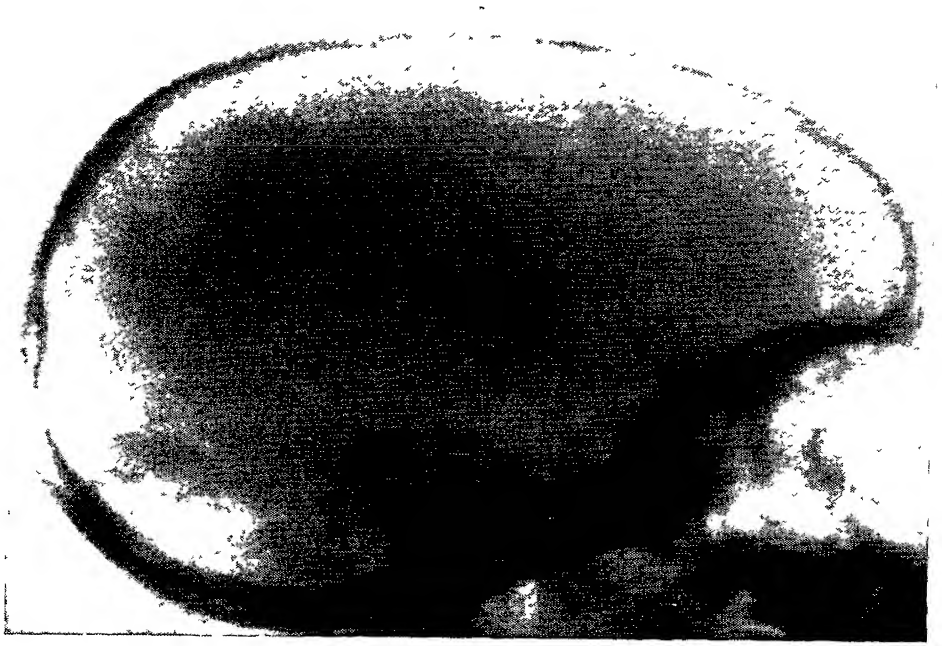


Fig. 37. Residual changes – calcification – in a child after tuberculous meningitis

Spinal Fluid

Normal (after Bürger)		In tuberculous meningitis
Appearance	Clear	Slightly opaque, fibrinous web appears at stagnation
Tension	60—200 mm m.c.	Increased
Cytosis	0-8/3	50/3 to 1,000/3
Protein, ‰	0.2-0.3	0.9 to 2
Pandy's test	Negative	Sharply positive
Nonne-Appelt's test	Negative	Sharply positive
Sugar, mg%	45 to 75	40 (traces)
Chlorides, mg%	700 to 720	560 to 580

Diagnosis. Apart from clinical symptoms, the pathologic changes in the spinal fluid described earlier with reduced sugar, cytosis and, especially, the presence of *Mycobacterium tuberculosis* are of major importance. Diagnosis is sometimes difficult, as it is necessary to differentiate from non-specific serous (benign lymphocytic meningitis, meningitis after parotitis) or purulent meningites, poliomyelitis and focal cerebral lesions (tumours, abscesses, etc.).

Treatment. In the early days of its therapy, tuberculous meningitis was chiefly treated by punctures combined with intramuscular streptomycin. Nowadays, non-puncture methods are preferred, and only in the severer cases a combination of intralumbar and intramuscular streptomycin (10 to 15 injections) is used together with phthivazid per os. Two basic drugs are used in non-puncture therapy—phthivazid perorally and streptomycin intramuscularly—and in some cases three (phthivazid, streptomycin, P.A.S.). In the severest cases, complicated with mental disorders, when the above treatment fails, the therapeutic complex may be successfully augmented by hormones, particularly the adrenocorticotropic hormone (ACTH), 10 to 20 units twice daily for 3 to 4 weeks.

If started early (at the 5-8th day after onset), treatment of meningeal cases will bring about improvement and subsequently complete clinical recovery. In certain cases, however, sclerotic or sometimes calcified residues remain (A. V. Alexandrova) (Fig. 37). On clinical recovery, chemotherapy should be continued for at least a year, mostly with phthivazid and P.A.S. In addition, the patient requires rehabilitation in sanatoria and subsequent regular follow-up treatment.

Tuberculous meningitis, earlier a lethal disease, can at present be cured by prompt specific therapy.

Chronic Hematogenous Dissemination

The chronic forms of hematogenous dissemination which arise after endogenous reinfection are genetically associated with acute miliary tuberculosis. In a good many pulmonary cases—20 to 30 per cent—such forms follow a benign course. The sick rate, apparently, may vary depending on factors influencing resistance, for instance, there was a marked rise of their incidence in wartime.

As regards anatomic substrate, all that has been said concerning exudative and, chiefly, productive processes, is valid here as well.

The importance of the chronic forms of hematogenous dissemination also lies in the fact that along with infiltrates these forms present the beginning of true phthisis. It is supposed, furthermore, that in its development from hemo-disseminated forms, fibrocavernous tuberculosis (phthisis) passes through a stage of infiltrative superinfection. As in miliary tuberculosis, we must emphasize the major diagnostic importance of properly interpreted radiography. Incidentally, it is correctly held that the onset of hematogenous dissemination is often revealed radiographically by a mere intensification of the vascular pattern, a more or less pronounced mottling developing later. Subsequently, in benign cases, these radiographic changes either disappear or are replaced by indurations.

As already stated, local hematogenous eruption is often observed in childhood simultaneously with or directly pending on primary infection. Such early dissemination, most probably, arises in the manner described, deriving its source from the glandular component of the primary complex. These minute tubercles, initially surrounded by perifocal inflammation, become entirely invisible after the latter resolves and appear on the radiograph only after subsequent induration and calcification. Very often these hematogenous tubercles form clusters about the hilus known as Simon's group metastases (Fig. 38). On a number of occasions only a sclerotic reticula or strands remain at the site of dissemination. Such fibrous transformation of early dissemination foci proceeds much faster than in the case of the primary complex proper, whose healing requires from 1½ to 3 years. The eruption is sometimes accompanied by extremely slight clinical symptoms such as lassitude, weakness and, very seldom, more pronounced malaise.

As regards the more extensive hematogenous lesions in adults, the comparatively equal size and, frequently, symmetricity of eruptions in bilateral lesions betray their hematogenous origin. Some patients do not notice the onset, their only complaint often being fatigue and, at times, moderate dyspnea at movement. Other patients reveal more pronounced symptoms (insomnia, tachycardia, anorexia). In a number of cases nervous hypersensitivity was accompanied by hypochondric conditions. Occasionally, the clinical picture resembled the less pronounced forms of basedowism. It happens, however, that a rather considerable eruption in the lung is observed in out-

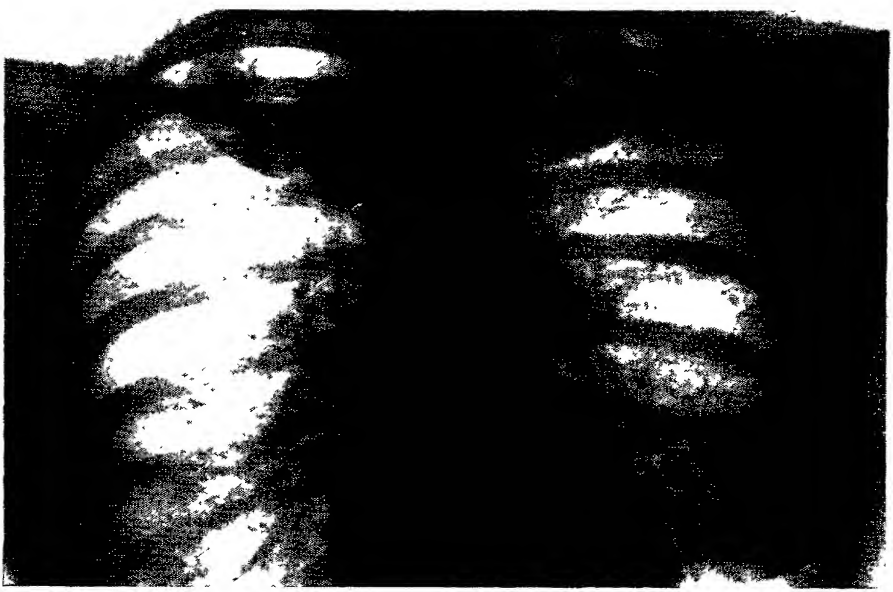


Fig. 38. Group metastatic foci in lungs apices

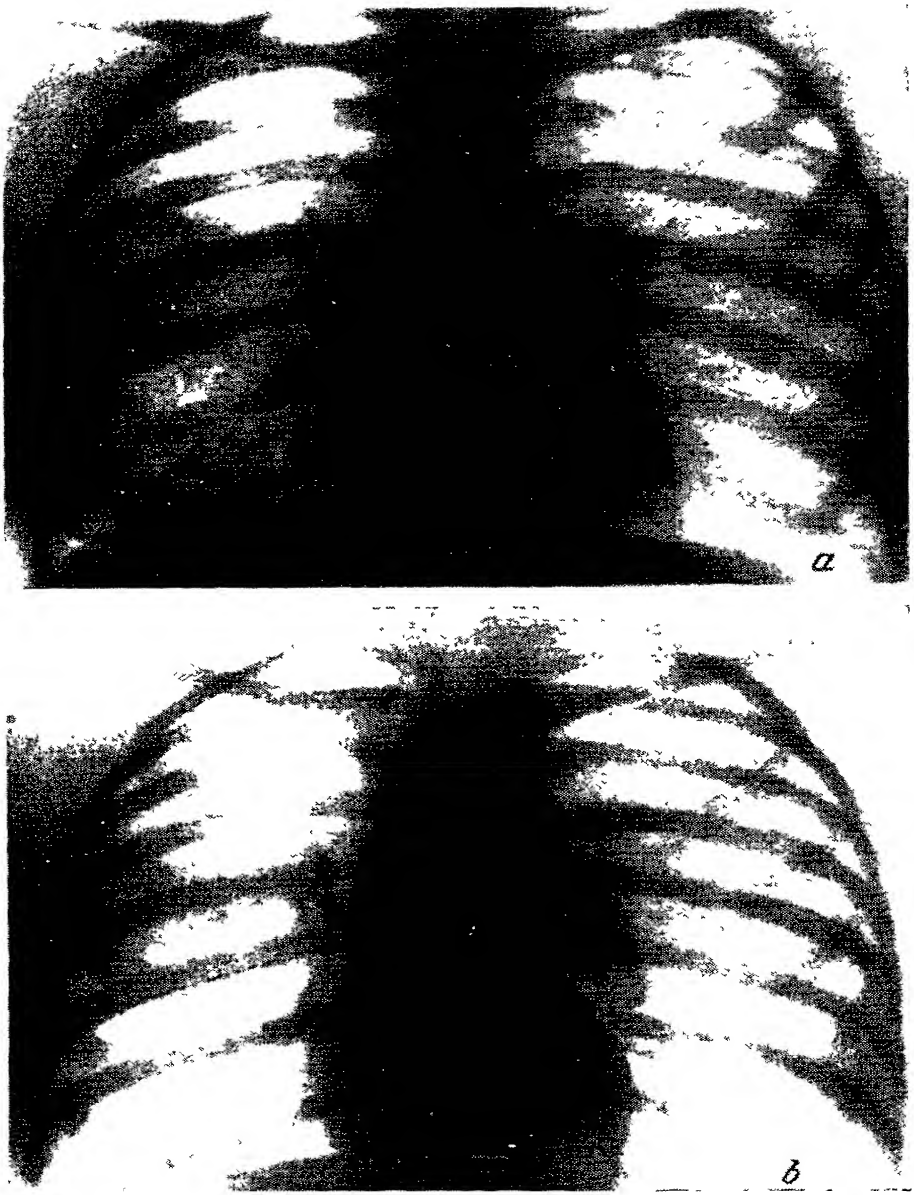


Fig 39. Lung X-rays of patient P

(a) before treatment, chronic pulmonary tuberculosis with hematogenous dissemination, *(b)* after antibacterial therapy, resorption of disseminated foci

wardly robust people, which is all the more important since in such circumstances it is easier to miss the precious moment when rational dietary and hygienic treatment alongside with chemotherapy can arrest further progression and bring about complete recovery.

Occasionally, the initial hemoptysis is followed by the appearance of diffuse foci occupying more or less extensive lung areas. There are cases when despite comparatively extensive lesions the physical symptoms are very slight, but there is notable dyspnea upon muscular exertion. The spleen, so often enlarged in miliary tuberculosis, is here seldom palpable. The patients show general weakness with subfebrile or normal temperature.

With a benign course, after 2 or 3 years, it is sometimes hard to detect the site of the lesion, which on other occasions is betrayed only by random petrifactions and reticular sclerotic changes (indurated areas). On the other hand, there are generally known cases of slow but sure progression.

In disseminated forms of tuberculosis, there are alternating periods of quiescence and exacerbation (wave-like course), which are believed to be occasioned by repeated bacillemia.

Attention has been drawn to the concomitants of such processes, viz., tuberculides, phlyctenulous conjunctivitis, *erythema nodosum*, which have already been dealt with earlier. As we now know, these symptoms may be the tuberculo-allergic concomitants of primary lesions in childhood. In certain adult cases of chronic dissemination, tuberculous metastatic foci were observed on the skin (*lupus vulgaris*), in the kidneys and urinary bladder, the bones and joints, serous membranes, inner ear, etc. In view of this, the presence of such lesions should give cause for comprehensive examination of the case in hand. It should also be remembered that the main concomitant of an initially unnoticed hematogenous pulmonary lesion may be tuberculous laryngitis. In more pronounced cases with a greater degree of pulmonary eruption, there is an impaired percussion note with a shade of tympany, radiography showing marked strands and finely mottled lung fields.

In early cases, hematogenous dissemination is accompanied by inflammatory changes in the pleura and, not infrequently, pleurisies with effusion, sometimes rudimentary. Recurrent diffuse bronchites with dry sibilant rales of different calibre, often mistaken for cold catarrh, are an occasional concomitant in such forms.

Occasionally, cavitation is observed, with a characteristic radiographic appearance of opacities of almost indefinable outline (so-called stamped cavities).

Diagnosis and differentiation. Data on the history, familial and environmental contacts, and previous tuberculo-allergic manifestations are extremely important. It should be remembered that initially im-

perceptible hematogenous dissemination is frequently accompanied by pleurisy with effusion. Out of 3,000 cases of pulmonary tuberculosis observed by the writer, largely with hematogenous dissemination, 10 per cent had a history of pleurisy with effusion. Subfebrile temperature and tachycardia, at times evoking a suspicion of endocarditis, on more detailed inspection and well-interpreted radiography may prove to be a result of hematogenous dissemination. Until the emergence of destructive changes, diagnosis is difficult owing to the absence of mycobacteria in the sputum and negligible physical findings. Depending on the stage of the disease, the blood picture is marked by a neutrophil shift to the left, monocytosis, a moderately accelerated E.S.R., and slightly modified proteinogram.

Prognosis and therapy. Chronic forms of hematogenous dissemination without marked destruction are readily amenable to hygienic and dietary treatment combined with continuous and systematic chemotherapy. Artificial pneumothorax is seldom used in these cases, the same applying to surgery. The following provides a demonstrative example.

Patient R.A., female, age 19, had bronchopneumonia on the right side in childhood. Repeated attacks of pneumonia at the same site in December 1953 and January 1954. In March 1954, pulmonary hemorrhage (100 ml of red blood) gave cause for hospitalisation. Contacts denied X-rays showed disseminated pulmonary tuberculosis General status at the time unsatisfactory, temperature up to 37 4-37.6°C in the evening, acute dyspnea, coughing with expectoration E.S.R. 37 mm per hour. Moist small-sized and dry rales in the basal section of the right lung. Sputum revealed *Myco. tuberculosis.* Radiography showed diffuse miliary densities in both lungs with a conglomerate in the basal section at the right (Fig. 39, *a*).

Treated by combined antibacterial chemotherapy (streptomycin 78 g, phthivazid 100 g) in urban and rural tuberculous hospitals. Chemotherapy resulted in total disappearance of intoxication, catarrh became inaudible, sputum grew negative. The lungs showed a residual reticular pattern, focal densities being no longer apparent (Fig. 39, *b*).

In March 1955, check-up showed complete well-being and 100 per cent occupational rehabilitation.

Conclusion: hematogenous disseminated pulmonary tuberculosis successfully treated by antibacterial drugs with complete resorption of pulmonar changes and recovery

FOCAL (NODULAR) PULMONARY TUBERCULOSIS

In the classification adopted in the U.S.S.R. focal tuberculosis is distinguished as an independent pathogenic form, although the genesis of the foci may vary. On a number of occasions small indurated and calcified foci may remain as residual changes in a clinically arrested and healed pulmonary process of exudative or productive nature. In some of these cases, the foci may be small and indurated, originating hematogenously and developing during primary infection or in connection with the primary complex. In adults they are usually residual, having no practical importance.

In cases with initial manifestations of active pulmonary tuberculosis in the form of soft minimal foci of exudative nature (G. R. Rubinstein and I. Y. Kochnova), these foci usually form in the upper part of the lungs, especially the apical segments, and are almost indistinguishable from the primary infiltrations described in the chapter on pathomorphology. The possible hematogenous origin of such foci should be considered as well. Provided adequate resistance and, particularly, prompt and rational treatment, they may either resorb or, with existing caseous changes, undergo fibrous transformation or even calcification.

With reduced resistance and hypersensitation, the foci may progress, increasing in size and disintegrating, i.e., behaving in the same manner as classical tuberculous infiltrations.

This form is classed separately for purely practical reasons, primarily the need to detect tuberculosis at the stage when changes are still limited and there is no destruction. It should be remembered that with lowered resistance even arrested and calcified foci may become a source of exacerbation. In such cases, the focus becomes decalcified, and we have even observed sequestration. V. G. Shtefko and A. I. Strukov have found on sectional material that in 12 per cent of all cases pulmonary tuberculosis developed out of such calcified foci through endogenous reinfection. In a number of cases, there may be subsequent development of tuberculous infiltration.

Diagnosis is confirmed by lung radiography, directed X-ray and tomography. At the early stage physical findings are absent. Occasionally, subfebrile temperature, a neutrophil shift and accelerated E.S.R. corroborate diagnosis.

TUBERCULOUS INFILTRATION

The newly elaborated concept of tuberculous infiltration, particularly that of its early form, brought about a radical change of outlook on the onset and evolution of tuberculosis. Earlier, it was considered incontrovertible that tuberculosis invariably begins in the apical area, which supposedly has a special preinclination towards tuberculous infection, and spreads craniocaudally, from storey to storey, in the form of caseous bronchitis and peribronchitis, progression being subsequently accompanied by destructive processes. The clinical picture was well described in classical handbooks as *phthisis pulmonum manifesta*–pulmonary consumption.

The advent of new examination technique, primarily dynamic radiological observation, dispelled a number of clinical delusions. In 1924, Assmann described a localised circular object visible on the background of a transparent lung field, mostly in the infraclavicular area, which he called an "early tuberculous infiltrate". Most of the cases in question were people earlier known to be absolutely healthy, but had maintained more or less close contact with open cases of pulmonary tuberculosis. This observation was confirmed by later

clinical findings, the tuberculous infiltration proving to acquire various forms and afflict individual segments or entire lobes (tuberculous lobitis). A morphologically essential feature, as stated earlier, is the combination of limited caseous bronchopneumonia with perifocal inflammation surrounding the caseous centre, this inflammation indicating pronounced allergy on the part of the patient.

A tuberculous infiltration is usually referred to the secondary period of infection, but there are cases of hilar infiltration whose centre is formed by caseated bronchial lymph nodes. Such changes mostly occur in childhood and adolescence, in the latter as a manifestation of late primary infection. These pictures were previously termed specifically—tuberculous infiltration—which emphasized the predominance of perifocal inflammation. Such hilar infiltrations, often with destruction, are occasionally associated with bronchial disintegration caused by spreading from caseous lymph nodes adjacent to the bronchi involved. This may likewise be accompanied by the development of bronchofistulous lesions which lead to bronchogenic metastases in the form of infiltrative and pneumonic foci.

Among the manifestations of secondary tuberculosis, we distinguish:

1. Localised tuberculous infiltrations—circular ("early");
2. Cloud-like infiltrations of pneumonic appearance;
3. Infiltrations involving entire lobes (tuberculous lobites);
4. Hilar infiltrations.

Frequently, such pulmonary lesions arise acutely, often as a pseudoinfluenzic syndrome accompanied by high temperature, in some cases with initial hemoptysis, at times, however, developing gradually.

The "early" circular infiltrations described by Assmann may be revealed only by prompt radiology, being inaudible stethacoustically. In a number of cases they are detected in group surveys through fluorography, especially large-film (Figs. 40 and 23, *b*). An acutely developing process is usually exemplified either by a cloud-like infiltration, or an extensive lesion involving a segment or lobe. We have frequently observed typical fan-like pictures of a tuberculous infiltration affecting the second segment of the right lung.

A tuberculous infiltration is marked by its tendency towards liquefaction associated with the presence of a more or less definite caseous focus. Disintegrating infiltrations are a frequent outcome of the evolution of such forms. Of course, disintegration (liquefaction, sequestration) is not inevitable under modern therapy, but the frequency of such evolution should be borne in mind when planning therapy for cases when the sputum or lavage reveals *Mycobacterium tuberculosis* and elastic fibres.

Diagnosis. Here, as usual, diagnosis is based on comprehensive clinical examination. In pronounced infiltrative changes accompanied by high fever, there is an impaired or even dull percussion sound

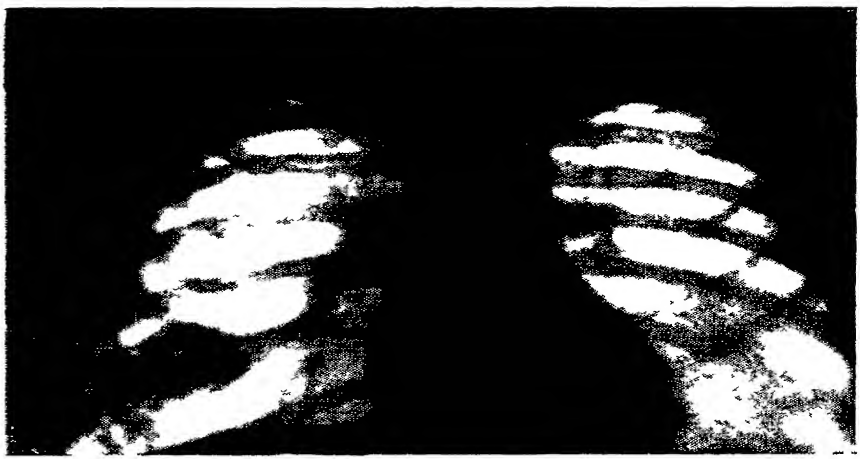


Fig. 40. Lung infiltration revealed by fluorography

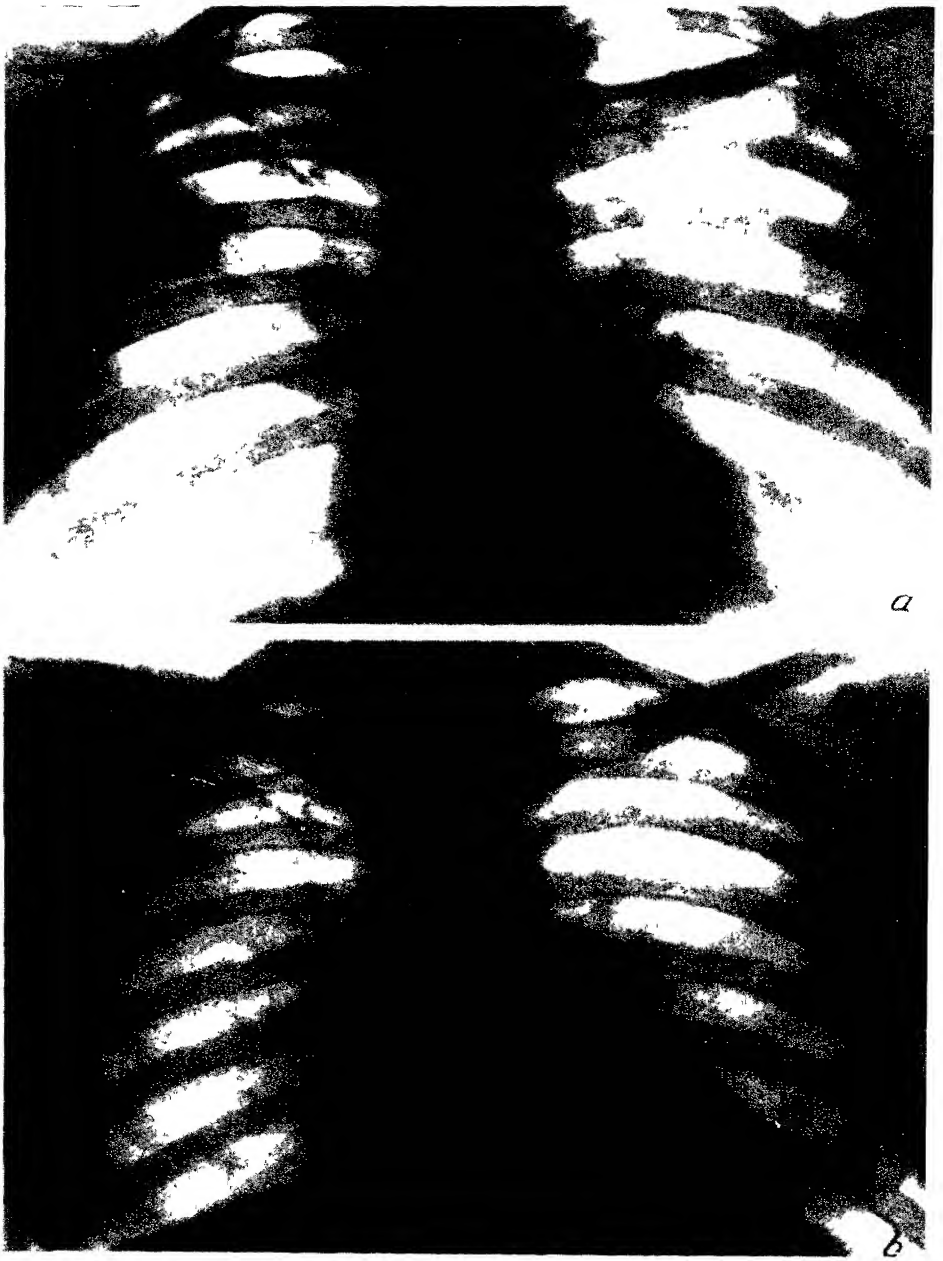


Fig. 41. Lung X-rays of patient S
(a) before treatment, early circular infiltration in right lung, *(b)* after antibacter therapy

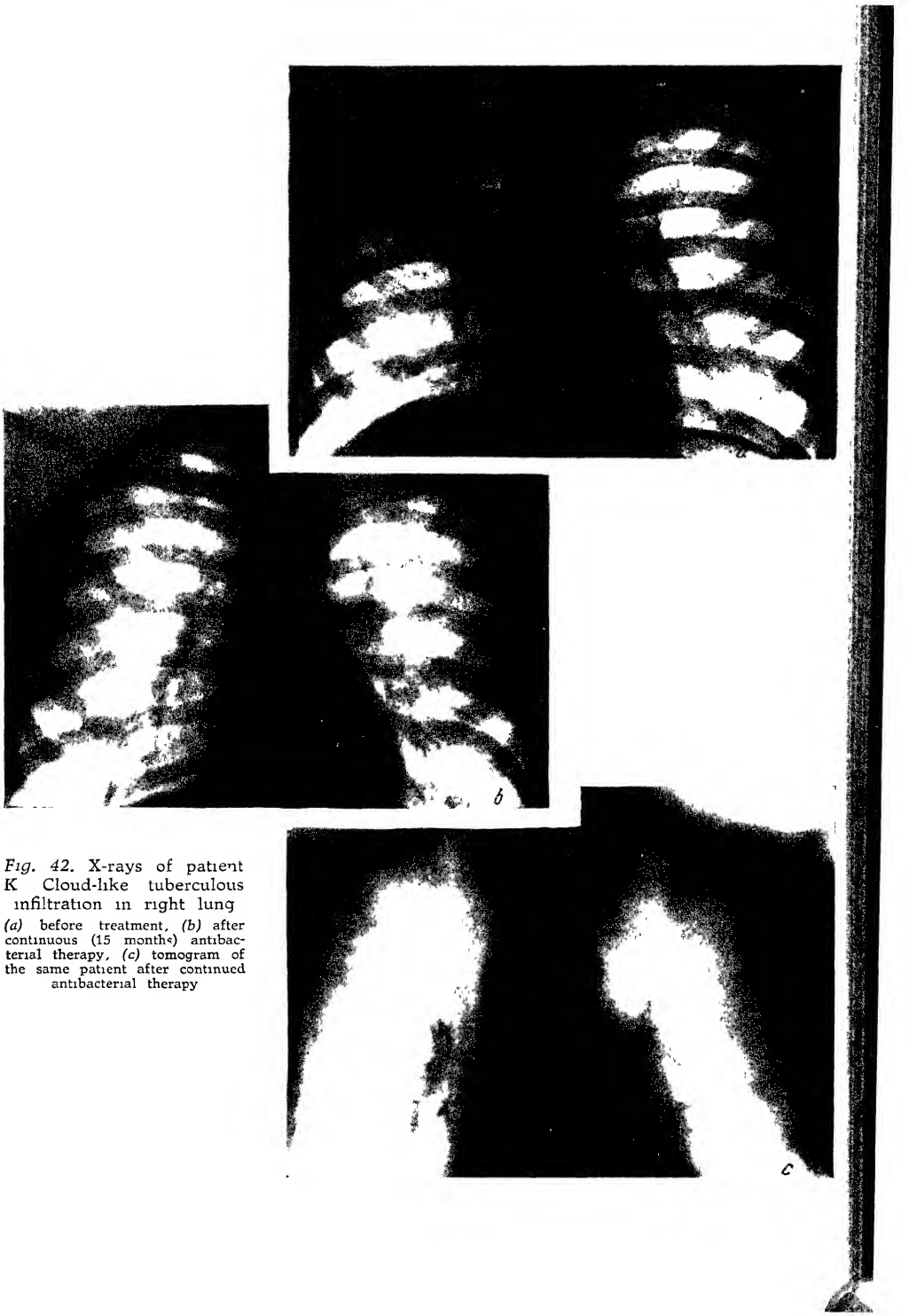


Fig. 42. X-rays of patient K. Cloud-like tuberculous infiltration in right lung
(a) before treatment, *(b)* after continuous (15 months) antibacterial therapy, *(c)* tomogram of the same patient after continued antibacterial therapy

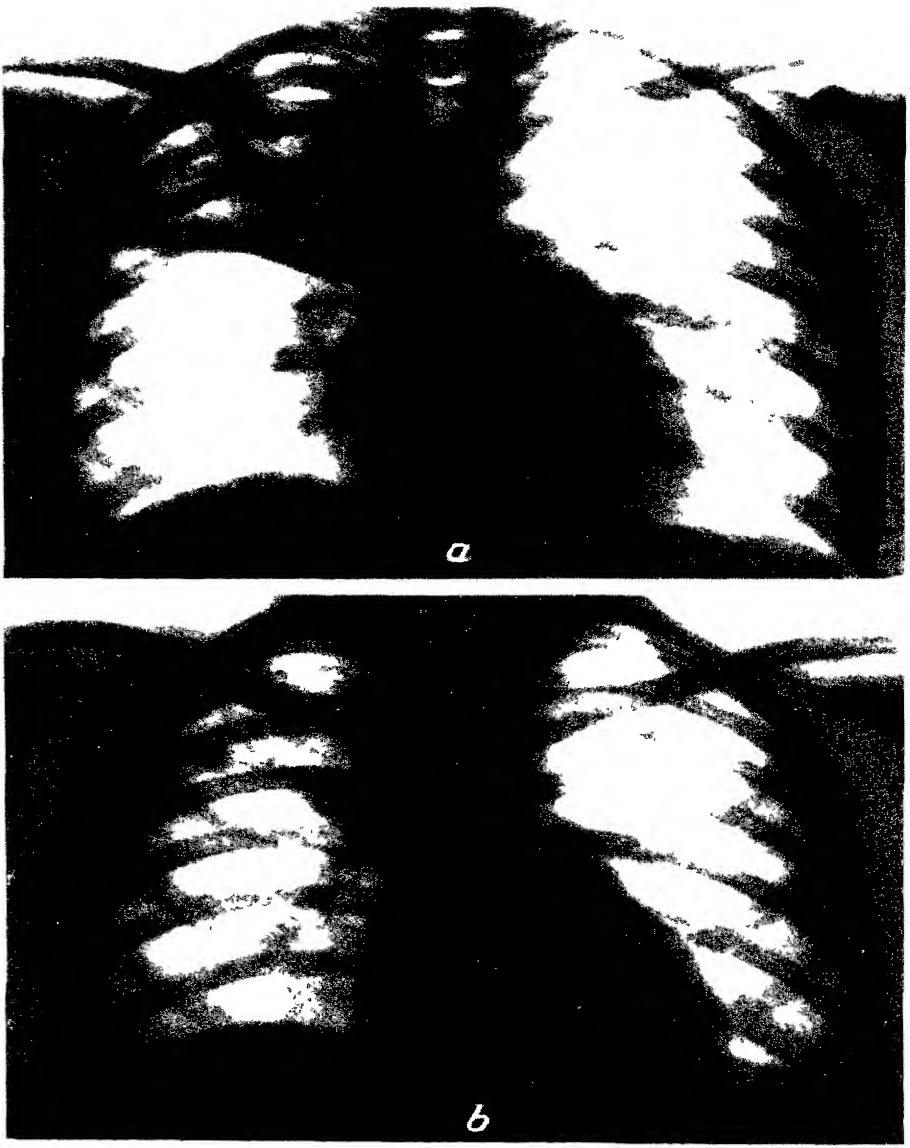


Fig 43 X-rays of patient X

(a) before treatment, tuberculous lobitis in the stage of disintegration and dissemination, *(b)* after 6 months of treatment

over the focus. The breathing may be harsh, with a bronchial shade, accompanied by small- and medium-sized moist rales, especially well audible in slight coughing at the level of the subsequent inhalation. With extensive destruction and cavitation, large-sized moist rales can be heard.

The acute stage is followed by quiescence which may begin even before the onset of perceptible resorption of the infiltration. In all such cases, especially with negative physical findings, radiology, as noted earlier, is the principal method for determining the clinical form of the disease and the nature of its evolution, especially destruction and cavitation, which is sometimes revealed only tomographically.

Difficulties of differentiation are often due to the similarity of the picture observed in atelectasis. In the latter, however, mediastinal displacement towards the afflicted area and diaphragmic elevation facilitate diagnosis. A localised circular density similar to a tuberculous infiltration is observed in peripheral carcinoma, adenoma, pulmonary gumma. Bronchogenic hilar carcinoma is also often similar to a tuberculous lesion. In such cases doubts are dispelled by the presence or absence of mycobacteria in the sputum, sputum cytology (atypical cells in neoplasms), age, and anamnesis (contacts with tuberculous patients).

Therapy. Under rational hygienic and dietary measures, initially with strict bed-rest and continuous combined chemotherapy, most cases of tuberculous infiltration terminate in clinical recovery with a cessation of bacillarity and resorption of the infiltrative lesions.

In cases of disintegration and cavitation, it is also frequently possible to achieve success by means of combined chemotherapy of sufficient duration—from 6-8 months to 1 or 2 years. If, however, the first months of treatment do not bring about closure, artificial pneumothorax or surgery are applied. This may be illustrated by clinical examples.

1 Patient S., female, age 45, had pneumonia in 1932 and 1935. In January 1959, had hemoptysis following influenza. At the same time tuberculous pneumonia was diagnosed. Contacts denied. On admission, her general status was satisfactory, temperature low subfebrile. E.S.R. 52 mm per hour; sputum concentration gave negative results. Harsh breathing in the upper lobe of the left lung. X-rays showed slight homogeneous density 3x2.5 cm in size at the level of the II right rib. (Fig. 41, *a*)

Three and a half months' clinical treatment included 35 g streptomycin, 64 g phthivazid, 730 g P.A.S. General condition showed considerable improvement, the patient gaining 12 kg in weight, E.S.R. falling to 8 mm per hour. Infiltration shadow in the lungs completely resorbed (Fig. 41, *b*).

On discharge, antibacterial treatment continued at local dispensary up to 12 months.

Conclusion: complete resorption of circular tuberculous infiltrate under antibacterial therapy.

2 Patient K.V., age 18, 10th-form schoolboy, in childhood had measles, whooping-cough, chicken pox, and pneumonia at the age of 10 and 11. Contacts denied. X-ray examination in January 1955 did not reveal pulmonary changes. Fell acutely ill in March 1955 with temperature up to 40.5°C, weakness, chills, nocturnal sweating. Tuberculous changes noted in right lung, for which the patient was hospitalised April

8, 1955 On admission, temperature low subfebrile, acrocyanosis, marked tachycardia; E S R 20 mm per hour Sputum revealed *Mycobacterium tuberculosis* In the right lung, small-sized moist rales Radiologically, the same area showed a fan-like non-homogeneous density diverging towards the periphery, with hazy contours (fan-like infiltration) (Fig 42, *a*)

Antibacterial therapy administered clinically (4 months) and extramurally (15 months), with a total of 65 g streptomycin, 200 g phthivazid, 3 kg P A S The result was complete disappearance of intoxication and rales in the right lung, E S R falling to 5 mm per hour Bronchial lavage negative Radiographically, small sclerotic foci in the infraclavicular area of the right lung (Fig 42, *b, c*). Total rehabilitation. Graduated school with a silver medal

Conclusion acute onset with febrile condition and an opaque tuberculous infiltration in the right lung, upper lobe, third segment Course altered drastically after treatment with a triple drug combination (streptomycin 1 g, phthivazid 1 g, P A S 10 g daily during the first two months of treatment; subsequently, phthivazid and P.A S for 13 months). Clinical recovery after 15 months' treatment

3 Patient H , female, age 19 No diseases in childhood Development normal. Contacts not established Ill since June 1958, complaining of cough, not treated In November 1958, temperature rose to 40°C with chill, shooting pain in the right hemithorax Penicillin did not reduce temperature In December 1958, infiltrative pulmonary tuberculosis of lobitic type in the stage of disintegration and dissemination was diagnosed at an antituberculosis dispensary. BK+EF+

Hospitalised December 26, 1958.

Temperature on admission 37 5°C. Pronounced flatness over the right lung corresponding in position to the upper lobe Bronchial breathing and moist rales of varying calibre audible in the same area. Radiography showed a marked density almost entirely covering the upper lobe of the right lung, sharply demarcated downwards along the interlobar fissure Two cavities denoted by opacities at the level of the clavicle and II rib. Soft focal shadows in the medial part of the left lung (Fig 43, *a*)

Treatment began with administration of streptomycin, phthivazid and P A S While in hospital, December 1958-June 20, 1959, received 184 g phthivazid, 28 g streptomycin and 2 3 kg P.A S Weakness and sweating disappeared Temperature normal Weight gain 2 6 kg. Auscultation revealed harshness over the upper lobe of the right lung Catarrh not demonstrated. E.S.R fell from 48 to 13 mm per hour. Bacillarity persisting, bronchial lavage positive. Radiology showed resorption of infiltration densities (Fig. 43, *b*). Only one disintegration cavity demonstrable tomographically, reduced four times

Conclusion. acute onset, with development of lobitis in the right upper lobe and two cavities. Continuous antibacterial treatment with a combination of three drugs (streptomycin 1 g, phthivazid 1 g, P A S 12 g daily) in the first month and later with phthivazid and P A S. arrested the process. One of the cavities healed, the other considerably diminished Later, lobectomy was performed

Antibacterial treatment continued

TUBERCULOMA

At one time, the term "circular tuberculous infiltrate" was applied to a variety of lesions which were not always homogenous anatomically, e.g., the above described cases of early infiltrations, as well as different forms of involution. Today, however, the so-called tuberculoma is distinguished as a specific clinical form, implying a limited circular lesion, more often solitary than multiple, having a diameter of 1 to 5 cm or even more. Such limited foci, which are described in the chapter on anatomy, are chiefly of two kinds—evolutive, i.e., progressing, often with a concentrically localised area of disinte-

gration, and involutive, or limited, with no manifestations of an active process. Anatomically, as stated earlier, the tuberculoma presents an incapsulated focus with laminary structure and central caseous necrosis. Small tuberculomata (within the limits of 1 to 2 cm) may be completely inert for many years, while larger ones may demonstrate exacerbation and disintegration even after many years of stability. Disintegration of a tuberculoma may be followed by bronchogenic metastases and pneumonic changes in other parts of the lungs.

Tuberculomata may develop as residual lesions after partial resorption of a tuberculous infiltrate, or following conglomeration of separate foci. In some cases, a tuberculoma develops in direct association with a primary pulmonary complex. The symptomatology of active tuberculomata includes intoxication, subfebrile or febrile temperature and pathological blood changes. In disintegration, which often arises eccentrically, the sputum reveals mycobacteria and elastic fibres.

Diagnosis, especially differential, often presents considerable difficulties, since almost identical radiological pictures occur in malignant pulmonary neoplasm, both primary and metastatic (bronchogenic carcinoma, adenoma). Similar pictures may be observed in cysts. Careful anamnesis and thorough examination of sputum (or, if absent, bronchial lavage) for mycobacteria, as well as cytological sputum studies, help diagnosis.

Prognosis and treatment. Quiescent tuberculomata may be practically non-apparent and, if small (1-2 cm in diameter), only require follow-up. In cases of active tuberculoma, especially with disintegration, segmental or bisegmental resection under cover of antibacterial therapy (streptomycin, P.A.S., phthivazid), which ensures favourable prognosis, is carried out. This may be illustrated by the following clinical observation.

Patient S.L., female, age 20. Family history favourable. Contacts denied. In childhood had measles, malaria, parotitis. At 18, after mental trauma, revealed duodenal ulcer and in August 1956, pleurisy with effusion in the right lung Two months later large tuberculomata with disintegration discovered in the right lung Tubercle bacilli non-apparent Periodic exacerbations treated with antibacterial drugs (phthivazid 45 g, P A S. 450 g, tubazid 9 g) Latest exacerbation occurred in July 1958. Pneumothorax could not be induced owing to obliteration of the interpleural cavity

On admission, general status satisfactory, temperature normal. Radiology revealed large disintegrating tuberculomata in the III and VI segments of the right lung (Fig 44, *a, b*). Mycobacteria not found Considering the patient's satisfactory functional resources and the nature of the process, resection of the III segment and subsegment was effected in the apical area of the lower lobe on November 26, after preliminary antibacterial treatment (streptomycin, 14 g, BEAMS, 154 g). Postoperative course smooth. Lung re-expanded completely (Fig 44, *c*) Intoxication completely disappeared. Smears from resected tuberculomata revealed tubercle bacilli Antibacterial therapy continued in sanatorium and later extramurally up to 12 months

Conclusion: when large tuberculomata with disintegration are discovered, surgery, and not chemotherapy, is preferable. In the cited case bisegmental resection led to clinical recovery.

CAVITATION AS A STAGE OF THE TUBERCULOUS PROCESS

The chapter on pathomorphology contains the basic data on the formation and evolution of tuberculous cavities. It should be recalled that disintegration may arise in any form of lesion, but is especially often observed in tuberculous infiltration. Disintegration and cavitation should properly be regarded as a stage of malignant development.

The recency or otherwise of cavitation is of major importance both from the clinical and therapeutic-amenability points of view.

Cavities are mostly observed from 25 to 40 years of age, i.e., in the prime of life. (Fig. 45). Early cavities, usually elastic, readily collapse. Older ones with fibrous walls or sometimes capsules collapse with difficulty. Thin-walled or so-called stamped cavities are mostly observed in pulmonary tuberculosis with hematogenous dissemination, apart from residual bullous and cystous cavities occasionally observed in clinical recovery from pulmonary tuberculosis.

As stated earlier, cavitation considerably complicates the course of the disease. Developing on a background of reduced resistance and hyperergy as a result of the liquefaction or sequestration of caseous foci, a cavity literally serves as a thermostat for tubercle bacilli. Out of 354 cases of cavitation which the author studied before the advent of chemotherapy, 331 (i.e., 93.5 per cent) revealed permanent bacillarity. Hence the major epidemiological importance of such lesions. Mixed infection, when the sputum contains both tubercle bacilli and pyogenic flora, is comparatively seldom of clinical importance. A cavity acts as a source of bronchogenic metastasis, tuberculous pneumonia and, occasionally, intractable progression. A tuberculous cavity with unobliterated vessels and an occasional Rasmussen's aneurism in the wall is the most frequent cause of hemoptysis and subsequent complications. In subpleural localisations, the process may spread into the pleura with the subsequent development of tuberculous empyema.

A cavity, if not closed spontaneously or healed by specific measures, is a constant source of exacerbation. In chronic pulmonary tuberculosis, bronchiectatic forms of cavitation are often observed. The condition of the cavity, its drainage, collapse and closure are linked with the condition of the draining bronchus, which may be seen on a properly developed lung X-ray or, occasionally, bronchographically, especially by segmental bronchography. Detailed description of a cavity, its walls and the surrounding tissue is extremely important for prognosis and efficacious therapy.

Symptoms of cavitation. Diagnosis should be carried out as meticulously as possible. Tympany in a secluded area of the lung, large-sized moist rales, particularly sonorous, and, occasionally, sibilant, and expectoration of bacillary sputum, especially with elastic fibres, are sufficiently clear symptoms of cavitation, but diagnosis may be verified beyond doubt only after radiological examination. A silent

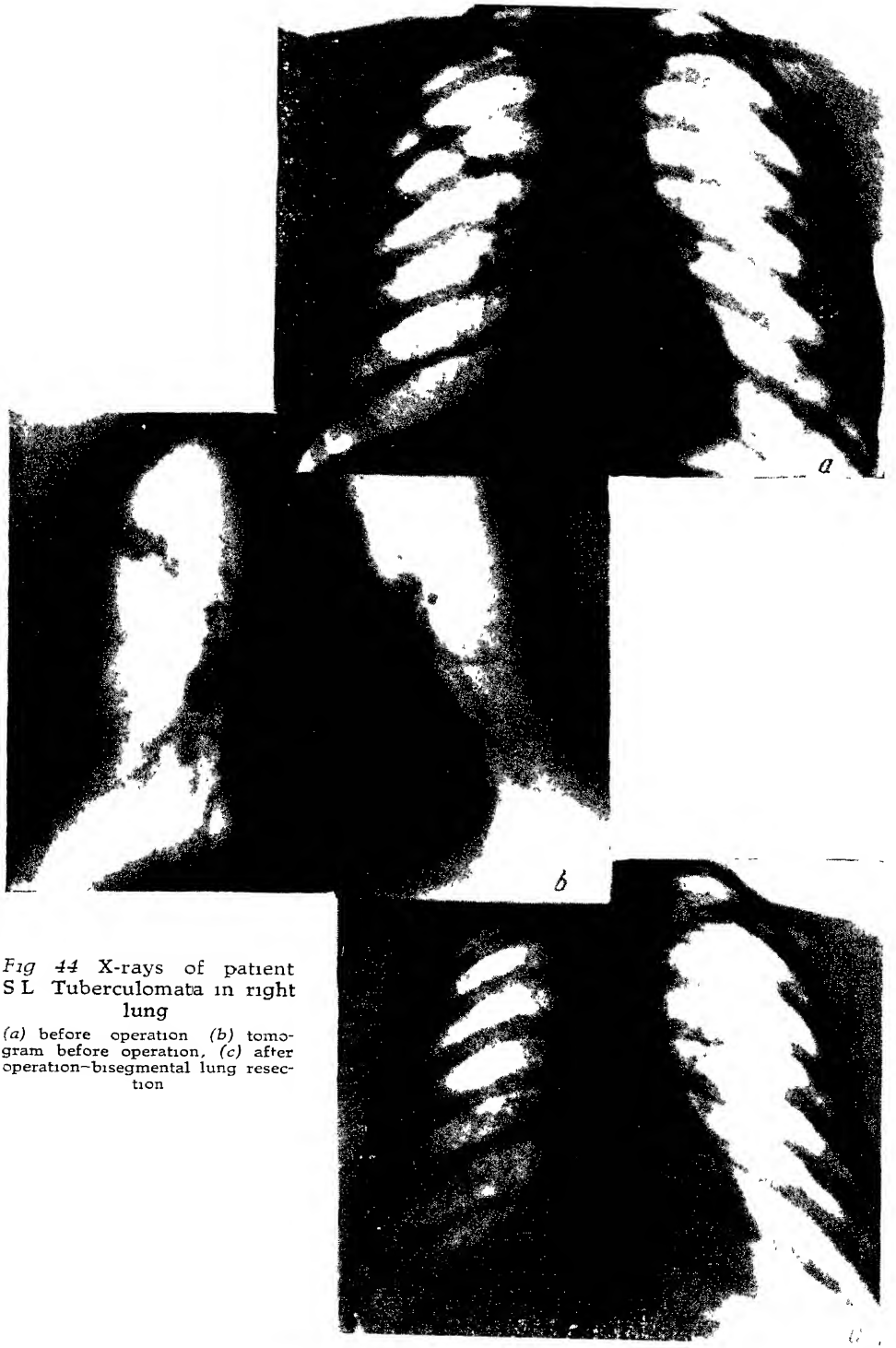


Fig 44 X-rays of patient S L Tuberculomata in right lung

(a) before operation *(b)* tomogram before operation, *(c)* after operation–bisegmental lung resection

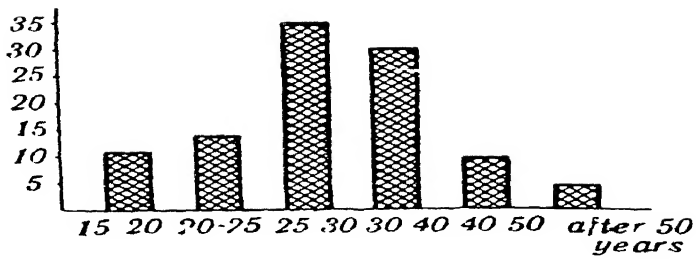


Fig 45 Age-distribution of patients with cavities (100 cases taken for autopsies)

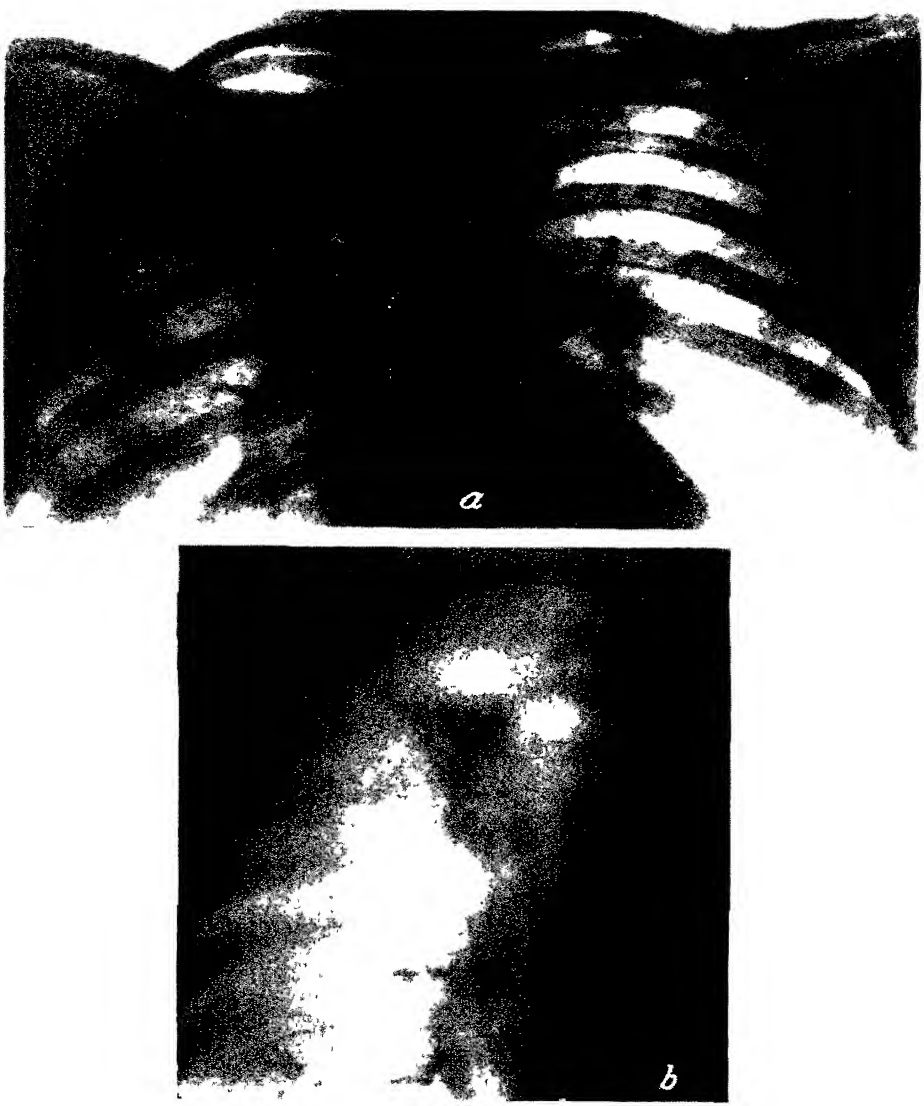


Fig 46 X-rays of patient R Infiltrative pulmonary tuberculosis with disintegration (fresh cavity) on the right
(a) before treatment, *(b)* tomogram of right lung, vividly showing cavity

Fig. 46

(c) after continuous (13 months) antibacterial therapy complete resorption of infiltration, cavity not discerned, *(d)* tomogram of the same case, star-like scar at site of former cavity

cavity is often well distinguished radiographically. Sometimes a cavity undetectable by conventional radiography may be revealed on a tomograph taken at the necessary depth (Fig. 29, *a, b*).

A diagnosis of cavitation determines the programme of therapeutic measures to be adopted by the physician. It should always be remembered, however, that cavitation is rendered possible by hypersensitation, healing depending on increased resistance.

The introduction of continuous antibacterial therapy offered new possibilities for the treatment of cavities. It enables fresh cavities to be often completely healed, closure being attained in 80 per cent of all cases. Here is an example:

Patient R Y, female, age 46, admitted prolonged contact with a nephew afflicted with the open form of pulmonary tuberculosis In childhood had measles and scarlet fever, at the age of 12—typhus, malaria In March 1957, developed malaise, weakness, anorexia and a cough Radioscopy revealed disintegrating infiltration in the right lung, the sputum being positive, for which she was hospitalised.

On admission, general status satisfactory, temperature low subfebrile, E.S.R. 35 mm per hour Small- and medium-sized moist rales on a harsh background in the upper lobe of the right lung Radiographically, the corresponding area showed a non-homogeneous density with an oval translucency in the centre connected through an opaque strip with the hilus (Fig 46, *a, b*) Antibacterial therapy continued for a year and two months (11 months institutionally and three months extramurally) with streptomycin (30 g), phthivazid (120 g), metazid (95 g), tubazid (40 g), and P.A.S (3 5 kg). As a result of therapy, intoxication symptoms disappeared, with a gain in weight of 11 kg, E S R. 10 mm per hour Catarrhal symptoms in the lungs became inaudible Radiology showed total resorption of infiltration shadows and a star-shaped scar at the site of the former cavity, confirmed tomographically (Fig 46, *c, d*). Two successive sputum tests employing cultivation gave negative results

Conclusion· infiltrative pulmonary tuberculosis successfully treated with antibacterial drugs administered for 14 months Healing of a fresh cavity by cicatrization. During the first month of treatment the patient received 1 g streptomycin, 0 9 g phthivazid, and 9 g P.A.S. daily; in the subsequent 11 months drugs of the isonicotinic acid hydrazide group (phthivazid, etc.) and P A.S. were administered.

CASEOUS PNEUMONIA

The classic forms of caseous pneumonia, especially bronchopneumonia sometimes involving entire lobes, occur comparatively seldom. Usually, they represent the culmination of long-standing cavitary tuberculosis. Acute forms, however, are also met, especially at primary infection in infancy. At present, though, such forms are rare. On a number of occasions they are associated with mycobacterial strains resistant to the basic antibacterial drugs (streptomycin and phthivazid). In adults the development of caseous pneumonia is accompanied by severe intoxication with high, often hectic, fever and initially resembles membraneous pneumonia. Profuse sweat and progressive cachexia are noted. Physical examination reveals confluent areas with moist and dry rales of varying calibre; the stethacoustic note in these areas, more or less widespread, is flat. The sputum, often

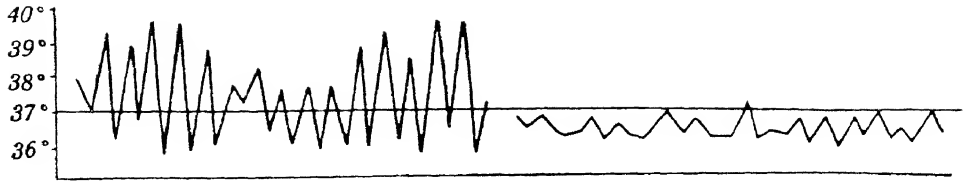


Fig. 47 Temperature curve of patient K. Caseous pneumonia

abundant (cavitation), contains mycobacteria. Severe intoxication is accompanied by a sharp neutrophil shift to the left and high E.S.R.

Previously, caseous pneumonia always terminated lethally, but now it is, to a certain extent, amenable to combined antibacterial therapy (streptomycin with phthivazid and P.A.S. intravenously). But in cases with dissemination, which testifies to reduced resistance and occasionally proceeds under negative anergy, the disease still remains extremely severe, prognosis being grave. The more benign form may be illustrated by the following:

Patient K., age 19, contacts not noted. Two years in his childhood were spent under extremely difficult conditions. Since 1953 works as a manual labourer. Fell acutely ill in November 1954, with temperature up to 39°C and pain in the throat. Hospitalised December 2, with a diagnosis of caseous lobular pneumonia and tuberculosis of the larynx.

On admission, general status extremely grave, marked cachexia, temperature of the hectic type varying from 36 to 40°C (Fig. 47). Tongue coated, dry. Daily sputum, up to 150 ml, revealed mycobacteria and elastic fibres. E.S.R. 60 mm per hour. Number of inhalations 28 per minute, pulse 100 to 120 beats per minute. Lung percussion revealed impairment in the upper segments of the lungs, mostly at the left, with harshness and numerous moist rales of varying calibre. Radiography revealed a non-homogeneous density in the upper lobe of the left lung with numerous translucences (Fig. 48, *a*). Laryngoscopy showed a widespread ulcerous-infiltrative lesion. Pirquet test negative.

Antibacterial therapy was administered for a 8 months with streptomycin (140 g), phthivazid (250 g), P.A.S. (300 g) under a general supportive regime. As a result, general condition improved considerably, temperature fell, E.S.R. diminished to 19 mm per hour. Pneumonic lesions in the lungs resolved; only a number of large encysted caseous foci remained, including several disintegrating cavities (Fig. 48, *b*).

Facultative bacillarity recorded, with clinical healing of laryngeal tuberculosis.

Conclusion: a case of caseous lobular pneumonia with a considerable lesion in the larynx and marked negative anergy. Eight months of antibacterial therapy led to termination of patient's extremely grave condition, the process assuming a chronic course (fibrocavernous tuberculosis).

FIBROCAVERNOUS PULMONARY TUBERCULOSIS

With inadequate body resistance, any form of the disease may develop into fibrocavernous tuberculosis, whose characteristic features are a tendency towards progression with bronchogenic metastasis (dissemination) and accompanying wasting. In the final period, there is a development of cachexia (*phthisis pulmonum*). Periods of exac-

erbation with fever, often hectic, with night sweating and anorexia, alternate with remissions, but subsequently the process usually progresses, often being complicated by late tuberculous lesions of the intestine (*phthisis intestinalis*) and larynx

The patient suffers from many complaints, including fever, night sweating, tachycardia, insomnia, abundant expectoration, frequently agonising cough upsetting night rest, at times overpowering cough apt to cause vomiting (irritation of the *n. vagi*). A frequent symptom are profuse cavitary hemorrhages which occasion fresh aspiratory bronchopneumonia and even widespread pneumonia of the caseous type. Such patients have an extremely characteristic appearance, often resembling the typical *habitus phthisicus*. In a number of cases the picture is that of classic pulmonary consumption.

Percussion usually reveals a more or less considerable impairment, sometimes with tympany; the breathing is bronchial or, with extensive organised cavities, amphoric. Varying moist rales, particularly large-sized, often sonorous, sibilant or rasping cavitary, fibrous changes and more recent radiographically revealed bronchogenic metastases, make up the syndrome of fibrocavernous tuberculosis. Quite often, the latter is accompanied by a bronchial lesion (bronchocavernous syndrome).

With the emergence of cachexia and complications, such as amyloid nephrosis often accompanying these grave pulmonary conditions, the prognosis is grave. Usually, it proves possible only to alleviate the sufferings by adequate care. This category of patients is of major epidemiological importance. Earlier, their life expectancy averaged from 4 to 5 years, but today, with the advent of antibacterial drugs which arrest exacerbation, it has been extended to 8 years and more. In chronic fibrocavernous tuberculosis affecting one lung, with satisfactory functional reserves, the method of choice is lung resection or surgical collapse (extrapleural pneumolysis or thoracoplasty).

The following clinical observation is an example of the successful use of chemotherapy (handicapped by streptomycin intolerance) in overcoming an infiltrative attack in a case of chronic fibrocavernous pulmonary tuberculosis.

Patient K., female, age 41, contacts unestablished. Born and brought up in good health in a rural locality. In February 1956 suffered from what was thought to be influenza. The morbid condition persisted for a long time. Radiology revealed fibrocavernous pulmonary tuberculosis in the stage of infiltration. BK+; EF+. Hospitalised February 28, 1956.

On admission, temperature 37.8°C, weakness, dyspnea, tachycardia, E.S.R. 57 mm per hour. Percussion showed impairment in the upper two-thirds of the right lung, with bronchial and broncho-vesicular breathing in the same area and moist rales of varying calibre. In the upper and medial lobes of the right lung, radiology revealed two cavities against the background of a non-homogenous cavity at the level of the first intercostal space and the frontal section of the IV rib. In the medial section of the left lung, small foci of bronchogenic dissemination (Fig. 49, *a*).

Therapy included a combination of larusan and P.A.S. An attempt to administer streptomycin resulted in a temperature rise of up to 39.5°C with tinnitus. After dis-

continuation of streptomycin the temperature instantly returned to normal Seven months of such treatment (larusan 170 g, P A S 2 kg) produced a marked clinical and radiological effect Intoxication completely disappeared. The patient gained 15 kg in weight. Temperature returned to normal. Mycobacteria and elastic fibres disappeared from the sputum Catarrhal symptoms no longer audible Breathing bronchovesicular. Radiology revealed complete resorption of infiltrative densities (Fig. 49, *b*) Only one cavity revealed tomographically in the apical area (Fig 49, *c*) On discharge, the patient was advised to continue chemotherapy under systematic dispensary follow-up

TUBERCULOUS PULMONARY CIRRHOSIS. BRONCHIECTASIS IN PULMONARY TUBERCULOSIS

Considerable growth of connective tissue may be observed both within and outside the affected lung areas, which is especially common, when the widespread application of chemotherapy has substantially prolonged the life expectancy of chronic cases.

Cirrhosis may arise in a variety of clinical conditions. Occasionally, diffuse cirrhotic changes emerge in hematogenous dissemination; more restricted retraction may occur in infiltrative and cavitary forms. Finally, with pleural involvement, there is pulmonary retraction accompanied by thoracic deformities and mediastinal displacement, or so-called fibrothorax. At later stages, cirrhosis is accompanied by the development of emphysema. In a number of cases, the connective tissue growths (pneumosclerosis) include areas of caseous necrosis and residual cavities. It is very often accompanied by bronchiectasis. Together with the reduction of functionally adequate parenchyma, the process tends to involve the pleura and the thoracic skeleton, which is most drastically disfigured on the same side as the prevalent lesion that affects the basic, i.e., respiratory, function of the lungs. The accompanying emphysema handicaps pulmonary ventilation. The peculiar vascular rearrangement with emptying of the pulmonary arterial system, hypertrophy of the broncho-arterial ramifications and an accompanying development of anastomoses between the mentioned two systems, hampers the aeration of the blood (A. I. Ryvkind). Such changes ensue as the result of prolonged chronic pulmonary tuberculosis. There are increasing circulatory difficulties in the lesser circuit accompanied by hypertension in the latter and followed in a number of cases by the development of what is known as a chronic pulmonary heart (*cor pulmonale chronicum*) with marked dyspnea, cyanosis and a characteristic electrocardiogram (Fig. 50). The described syndrome may be illustrated by the following case which terminated in death.

Patient K. M., age 41. Diagnosis widespread chronic fibrocavernous tuberculosis with a giant cavity in the upper lobe of the right lung, cirrhosis and pleural involvement; marked pulmonary emphysema, cardiopulmonary insufficiency of the III degree, *cor pulmonale chronicum.* Ill with tuberculosis for 9 years. Condition severe, dyspnea, cyanosis, edema

Electrocardiography on admission. synovial rhythm 120 per minute, P-Q interval 0.15 sec., QRS complex 0.07 sec, QRST 0 32 sec, systolic index 64 (normal 52).

Fig 48. X-rays of patient K.
(a) before treatment, caseous pneumonia, *(b)* after 8 months of antibacterial therapy

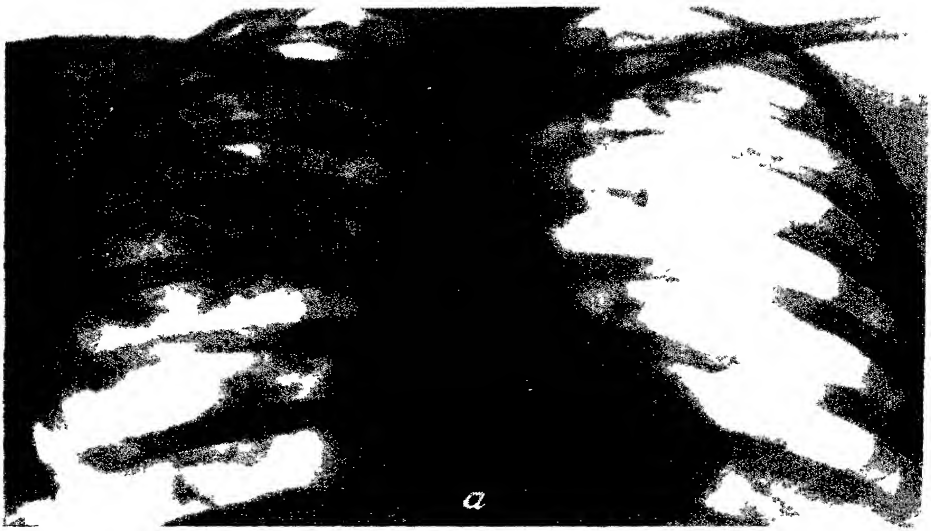


Fig 49. X-rays of patient K V.
(a) before treatment, chronic fibrocavernous pulmonary tuberculosis in the stage of infiltration and dissemination

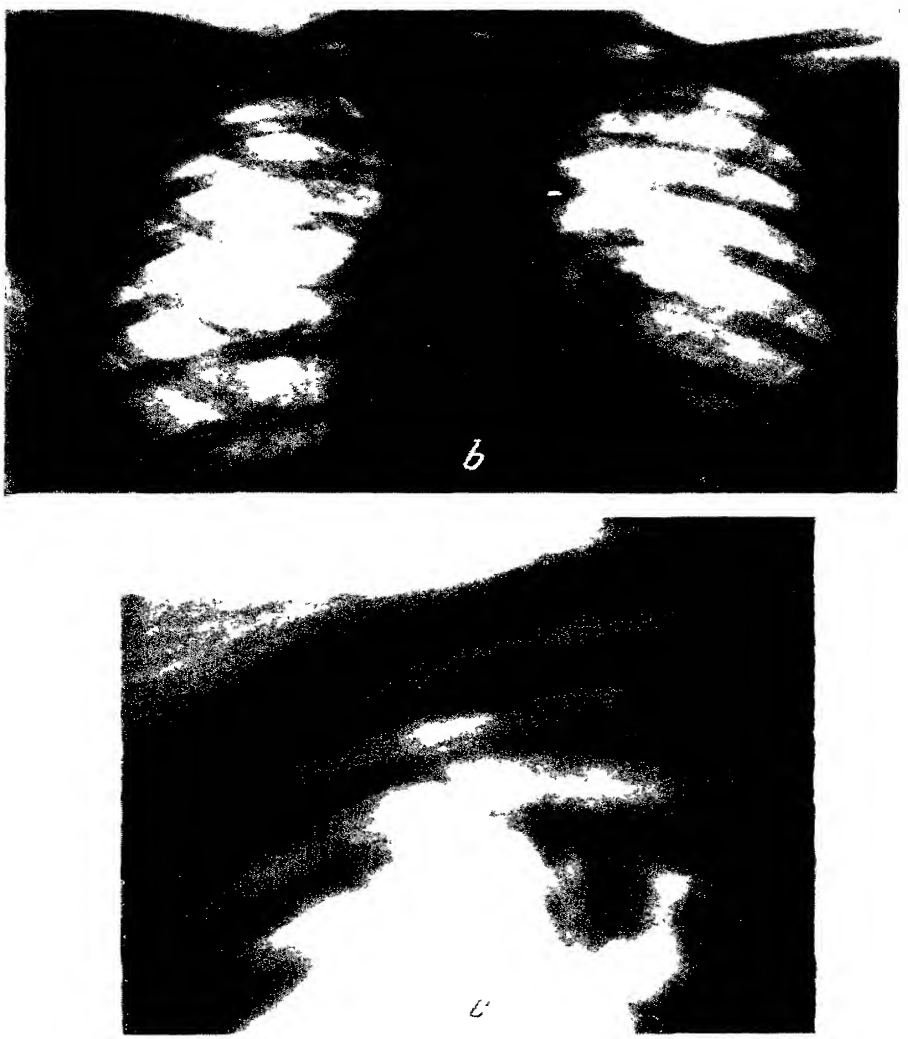


Fig 49b (b) X-rays of the same case after antibacterial therapy; *(c)* tomogram of the same patient after antibacterial therapy

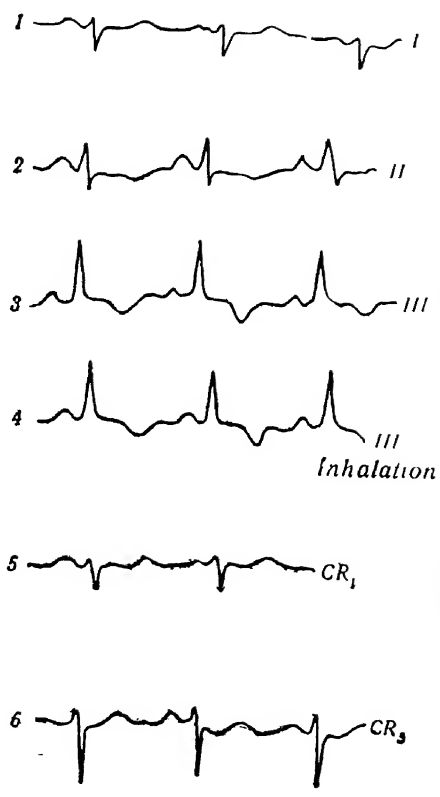


Fig 50 Electrocardiogram of case with chronic pulmonary heart due to tuberculous pulmonary tuberculosis

(1) deep teeth S, low teeth R *(2)* two-phase teeth T high teeth P, *(3)* high teeth R, negative teeth T, high teeth P, *(4)* the same as in Lead III *(5)* and *(6)* deep teeth S, low teeth R

Fig 51. Tuberculosis pulmonary cirrhosis with concomitant emphysema

Low voltage in teeth R, high tooth P in Leads II and III. Right graph: low S-T interval in Leads II and III and at aspiration

Fifty-three days after hospitalisation the patient died with mounting cardiac insufficiency.

Conclusion: *Cor pulmonale chronicum.*

Autopsy findings giant cavity in the right lung, random caseous necrotic foci in both lungs; obliteration of pleural cavities; pleuropericardiac adhesions on both sides; sharp hypertrophy of the right ventricle and dilatation of its cavity; parenchymatous dystrophy of the cardiac muscle.

With the development of massive retraction after pleurisy with effusion, the organisation of residual changes, as noted earlier, is accompanied by considerable mediastinal displacement towards the affected side and drastic thoracic deformation with rigidity of the affected side. The described syndrome is known as fibrothorax, often accompanying the respiratory and circulatory changes described above.

Diagnosis and differentiation. Diagnosis in these cases is not difficult, the anamnesis, clearly demonstrating the typical course and evolution of tuberculosis. The incidence of mycobacteria (present or past), absence of atelectatic symptoms (in fibrothorax), with concomitant bronchiectases and earlier described functional disorders, are helpful in drawing up a correct conclusion.

Treatment. It should be borne in mind that patients with lung cirrhosis and bronchiectasis gradually develop into cardiac, rather than pulmonary, cases. Apart from conventional dietary and hygienic measures, depending on the general condition, the measures described in the chapter on symptomatic therapy should be resorted to. Cardiac drugs, oxygen therapy (inhalation) and—in indicated cases with acute congestive symptoms—bloodletting, serve to alleviate the condition during decompensation. Fig. 51 illustrates the radiological picture in tuberculous pulmonary cirrhosis.

PLEURISY OF TUBERCULOUS ORIGIN

In the majority of cases pleurisy with effusion accompanies pulmonary tuberculosis. Often, however, it arises even earlier than a pulmonary lesion may be detected radiologically. In childhood and adolescence, pleurisies occasionally develop in connection with tuberculous lesions of the hilar lymph nodes. Clinically, such cases should be viewed as attacks of tuberculosis. Such pleurisy is very frequently associated with hematogenous dissemination.

Clinically, three main types of pleurisy are distinguished: (1) dry and fibrinous; (2) with effusion; (3) purulent.

In a number of cases pleurisy with effusion is the first sign of pulmonary tuberculosis. According to the author's own findings, after pleurisy, the open form of pulmonary tuberculosis developed within one year in 40.3 per cent of cases, within 1 to 3 years in 13.6 per cent and after 3 to 5 years in 6 per cent of all cases. A clear picture of pulmonary tuberculosis preceding pleurisy was recorded in 19.3

per cent. This emphasises the need for periodic X-ray control of post-pleuritic cases at least 3 to 4 times a year for no less than three years.

Dry pleurisy begins with sharp, shooting pains in the lateral section of the thorax, hindering free respiration. Coughing and febrile conditions with temperature up to 38°C and more are notable. Physically, there is sometimes no pathology except the sound of pleural friction. Radiology may reveal no foci in the lungs except for occasional apical lesions. Usually, the disease continues for several days. The pain may irradiate into the abdominal cavity as, for instance, in diaphragmic pleurisy. On many occasions, dry pleurisy may recur.

Treatment. Rest with even bed-warmth, alleviation of pain by *Codeini phosphorici,* 0.02 g two or three times daily or occasional injections of pantopon. Diverting therapy: compressive bandage on affected area (better with warm vegetable oil) and, if indicated, phthivazid in a dosage of 1 g daily; P.A.S. 12 g per day. On some occasions the picture of fibrinous (dry) pleurisy merely presents the initial stage of classic tuberculous pleurisy with effusion.

Pleurisy with effusion (*exudative-serous pleuritis*) often begins as an acute febrile disease, with temperatures frequently as high as 39°C and more and shooting pain in the thorax, disappearing with the accumulation of exudate. The pulse is accelerated, occasionally with respiratory arrythmia. Percussion reveals a marked dullness demarcated upwards by the Damoiseau line, indicating the presence of exudate in the pleural cavity. The radiographical picture (Figs. 52, *a* and 52, *b*) is extremely demonstrative. Palpation shows reduced vocal fremitus in the area of dullness, impaired breathing being audible stethacoustically. Above the fluid level one is apt to observe tympany due to relaxation of the pneumoparenchyma. Extensive fluid accumulation is accompanied by a displacement of the mediastinal organs towards the unaffected side.

To determine the nature of the exudate, which is the factor most significant for the choice of therapy, a pleural puncture is made, strict precautions being taken against the penetration of air into the syringe. In indicated cases, e.g., with large accumulation of fluid, displacement of mediastinal organs and dyspnea, the fluid is evacuated.

The serous exudate has a straw-yellow or greenish colour, sometimes opalescent, with a specific gravity of 1015 to 1020. With transudate, the specific gravity is usually below 1015. Exudate is richer in protein than transudate. By means of Rivalta's test (a drop of exudate in a solution of acetic acid leaves a cloud-like opacity), the protein content is found to be 2.5 to 7 per cent, whereas in transudate (hydrothorax) there is 0.2 to 0.3 per cent of protein. Mycobacteria are seldom revealed in the exudate by direct smear, their presence being mostly determined by cultivation or guinea-pig inoculation.

An accelerated E S R. and a shift to the left are highly characteristic of pleurisy with effusion. It should be noted that the exudate

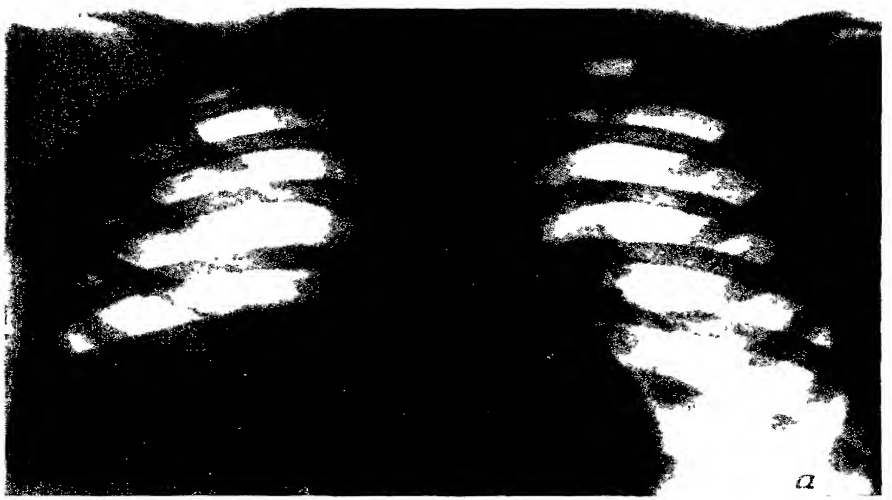


Fig 52a Lung X-rays of case with pleurisy with effusion in the right lung

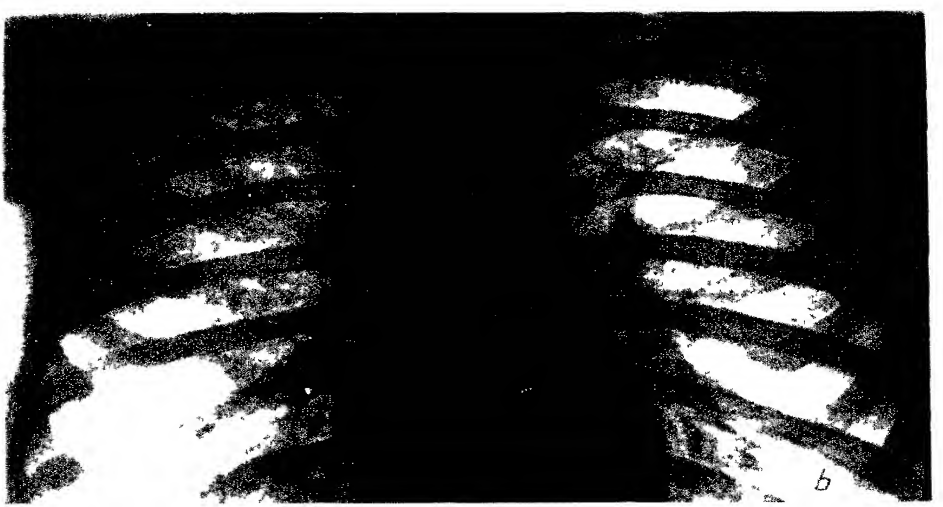


Fig. 52b X-rays of the same case three years later Bilateral pulmonary tuberculosis with hematogenous dissemination

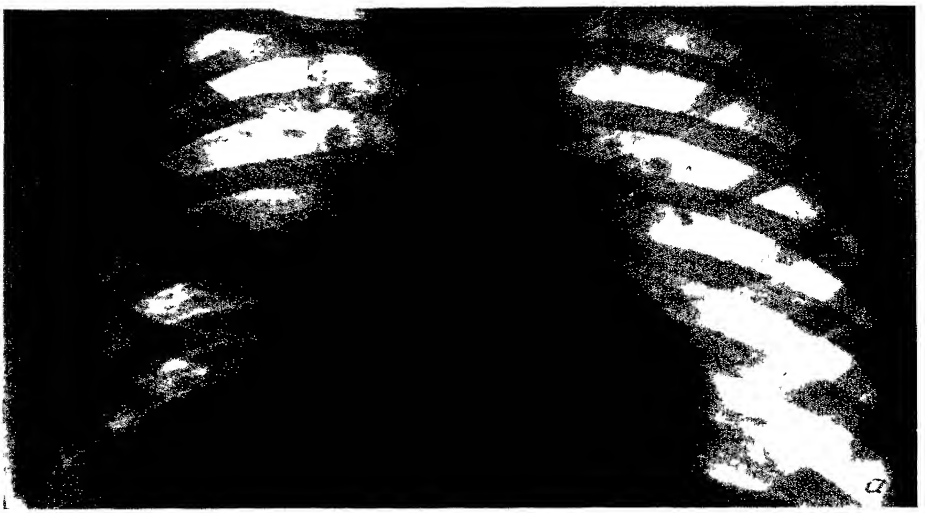


Fig. 53a X-rays of interlobar pleurisy of the right lung (spindle density)

Fig. 53b The same in laterography

is sometimes localised in the interlobar fissure, radiologically presenting a spindle-like density (Fig. 53, *a*) which is extremely instructive in laterography (Fig. 53, *b*).

The course in pleurisy with effusion is of greater duration than in the dry variety, taking from 3 weeks to 2 or 3 months. The temperature falls gradually, lytically.

Treatment. Strict bed-rest is prescribed, with a rational diet poor in sodium chloride and rich in vitamins. Chemotherapy is obligatory. At first, in the acute stage, streptomycin is prescribed in doses of 1 g intramuscularly, as well as phthivazid 1 g and P.A.S. 12 g daily. In the 2nd and 3rd months the dosage is 1 g phthivazid and 12 g P.A.S. The treatment should be continuous, especially with marked pulmonary changes. Available experience suggests that, along with antibacterial drugs, ACTH should be used in a dosage of 20 units twice daily, provided that the Thorn's test has proved positive

Purulent pleurisy in pulmonary tuberculosis is mostly associated with previous inductions of artificial pneumothorax, occasionally applied unnecessarily, sometimes at the patient's personal request, and continued for several years. In most of the author's observations he had to deal with perennial pneumothorax (5 to 10 years) causing a drastic shell-like pleural consolidation which hindered re-expansion of the lung. The ensuing picture was that of rigid pneumothorax with purulent pleurisy—pleural empyema.

In the acute period of this grave complication, systematic evacuation of the exudate under cover of penicillin and streptomycin therapy sometimes succeeds in changing the exudate from purulent to serous, the purulent fluid often being a product not only of tuberculous, but of pyogenic infection. Active hermetic aspiration of the pus promotes re-expansion of the lung and absorption of the exudate. In cases of drastic pleural thickening, radiologically shown to be utterly unamenable, it is useless to prolong conservative treatment. In such cases only surgical intervention—decortication with pleurectomy—leads to re-expansion and elimination of pleural empyema. The operation is grave but essentially restorative, producing good results if a correct choice of patients in a generally satisfactory condition has been made.

CHAPTER VIII

DIAGNOSIS OF CLINICAL RECOVERY

Contemporary combined therapy, incorporating the use of powerful drugs under rational general supportive measures, in many cases brings about recovery from tuberculosis.

Combined therapy rather quickly leads to the resorption of fresh hematogenous miliary tubercles, provided that vascularisation is still adequate and ensures circulation in the affected lung areas. Other therapeutic effects include the disappearance of infiltrative pneumonic lesions in the lungs and, on many occasions, the collapse and closure of cavities and healing of affected bronchi. In cases with caseous necrotic foci, however, resorption may only be partial. In such patients the most common development is fibrous transformation, incapsulation and walling-off of the respective foci.

The process is arrested, intoxication discontinues, and mycobacteria cannot penetrate from the incapsulated foci into the surrounding parenchyma and bronchi ("focal stabilisation"). This may not be regarded as total recovery, but only as a stabilisation under which pathological manifestations cease and the patient's energies are restored. The patient is thereby provided with sufficient power of adjustment to environmental requirements, particularly to work. Occupational rehabilitation is quite often limited, but the patient is still left a sufficiently broad field of endeavour. A properly organised rehabilitation scheme helps the convalescent or post-convalescent to choose easier occupational conditions or a different profession. Under such circumstances, even with incomplete recovery, there is a certainty of prolonged compensation despite the presence of residual changes in the lungs.

What are these residual changes and what is the prognosis when they are present? In almost 20 per cent of all cases therapy brings about complete recovery either without any traces in the affected lung or with scars. Of course, there are no functional disorders in such cases. Wherever the residual organic changes include sclerosis, as well as indurated and incapsulated minimal foci, recovery may also be considered sufficiently stable.

In cases of more pronounced residual changes with focal inclusions in the fibrotic areas and functional disturbances on the part

of the nervous system (vegetative dystonia) and pneumocardiac system, prognosis should be appraised more cautiously. Clinical recovery may be stated with assurance when the results of treatment have been proved by time, viz., in the author's view, not earlier than two years after cessation of bacillarity, normalisation of temperature and restoration of general functional well-being.

When returning the patient to occupational activity, it is important, of course, to assess the stability of achieved results, for which the physician should be able to differentiate the residual changes. Dynamic follow-up with thorough clinical and radiological control, revealing a stable cessation of bacillarity and a return of the blood picture to normal, assists in making a conclusion. In his personal practice, the author applies the table of residual changes reproduced in the appendix (p. 195) which includes the following basic divisions:

1. Complete recovery with full rehabilitation;
2. Recovery with radiologically determinable limited changes in the lungs, often assuming the form of scars, without functional disorders and with occupational rehabilitation;
3. Recovery with more pronounced sclerotic changes including residual foci, moderate functional derangements and more or less limited rehabilitation.

The table includes also a fourth group of cases in which tuberculosis as such has been cured, but marked residual changes of non-tuberculous nature are apparent, e.g., pulmonary retraction, pneumosclerosis with bronchiectases and, occasionally, disturbances of cardiac activity associated with overload of the right heart. Here we have to reckon with considerably limited rehabilitation, referring such post-convalescents to invalid status. As regards the special group of patients subjected to surgical intervention, here, of course, we also meet representatives of all four grades—from complete recovery to cases with residual changes coming under the fourth group.

The diagnosis of clinical recovery is based on assessment of all objective clinical and radiological findings obtained under dynamic extramural follow-up.

Clinical recovery is stated after:

1. Stable cessation of bacillarity;
2. Return of temperature to normal;
3. Stabilisation of weight;
4. Normalisation of the blood picture (E.S.R. and hemogram);
5. Rehabilitation.

On the part of the lungs, there should be:

1. Cessation of coughing;
2. Disappearance of classic physical manifestations indicating inflammation and destruction;
3. Stabilisation or absence of the earlier described residual changes, revealed at periodic follow-up by means of radiography and serial tomography.

A diagnosis of recovery is no reason for discontinuing after-care, but merely serves as grounds for transferring the patient to the III group of dispensary notification, denotification being effected only after the achieved results have been sufficiently proved by time.

On denotification, the post-convalescent is prescribed an adequate regime including occupational activity and mandatory rest during the day, if conditions allow, the days off being spent out-of-doors.

Irregular life, violations of the prescribed routine, alcohol and smoking frequently lead to relapse.

CHAPTER IX

DIFFERENTIAL DIAGNOSIS OF PULMONARY TUBERCULOSIS

There are several occasions when the differential diagnosis of pulmonary tuberculosis presents certain difficulties.

They may appear at initial stages of the disease in childhood and adolescence, when the patient reveals only general symptoms, localised lesions being undemonstrable. Occasionally, difficulties arise when interpreting lymphatic changes in order to differentiate between tuberculous lymphomata, lymphogranulomatosis and sarcoidosis.

It is hard to determine the etiology of pulmonary infiltrations when the sputum shows no evidence of mycobacteria. In some cases a solution may be obtained only by thorough dynamic observation, e.g., in transient eosinophilic infiltrations of the Loeffler type, which may sometimes take several days.

It is particularly difficult to differentiate between certain forms of pulmonary tuberculosis and carcinoma, e.g., tuberculomata and circular peripheral cancer, disseminated and cavernous forms of cancer of the lung, etc. Here meticulous technique is of major importance. Anamnesis should be effected with the utmost thoroughness, checking the findings against documental data. Correct orientation is facilitated by lung radiography, comprehensive physical and laboratory studies with the use of the most up-to-date methods (tomography, bronchoscopy and bronchography, bacteriological and cytological methods of sputum examination, with occasional biopsies of pathological organic changes). To emphasise the importance of adequate technique in differential diagnosis, including the extensive use of radiological and clinical methods, we shall examine the difficulties arising in diagnosis under the following headings:

1. Disseminated pulmonary lesions;
2. Parenchymal thickening;
3. Parenchymal softening;
4. Bronchial lesions;
5. Conditions involving the intrathoracic lymph nodes;
6. Parasitic diseases.

DISSEMINATED PULMONARY LESIONS

In disseminated pulmonary lesions, distinction should be made between acute forms, chronic cases and camouflaged, symptomless processes. Diagnosis of miliary tuberculosis is seldom difficult. In this form, the general condition is severe, with temperature reaching 40°C and more, dyspnea and cyanosis. A well-developed radiogram shows disseminated minimal foci over the entire pulmonary area, which are smaller in productive forms and somewhat larger in bronchopneumonia. At times, these disseminated foci radiographically resemble snow-flakes. Similar pictures may likewise occur in miliary carcinosis which, however, is more commonly marked by the lack of fever, the presence of dyspnea with a low febrile temperature and an absence of the historic data usual in tuberculosis (family cases or past disease in the patient proper). In childhood, miliary tuberculosis occasionally develops at the stage of early generalisation—in the primary complex period. In adults, one should carefully examine the condition of the intrathoracic lymph nodes, remembering that any other tuberculous focus, especially caseous, may be a source of bacillemia and dissemination. Thus, for instance, we have observed postoperative development of miliary tuberculosis at epididymitis.

It should be borne in mind that in approximately 40 per cent of cases miliary tuberculosis is accompanied by the meningeal localisation—basilar meningitis—whereas diffuse forms of pneumocarcinoma produce metastases in the central nervous system much less frequently. Careful analysis of the blood is a great help in diagnosis. In miliary tuberculosis there are frequent manifestations of leuko- and particularly lymphopenia. At present, under specific antibacterial therapy, intoxication is rapidly arrested in miliary tuberculosis, and the radiographically determinable foci resolve and disappear in 1 or 2 months, which is not the case in carcinosis.

In chronic forms of dissemination, apart from hematogenous tuberculous dissemination, allowance should be made for the possibility of such diseases as Boeck's sarcoidosis in its miliary stage. Under careful observation, if material on onset and evolution, especially X-rays, is available, it is possible to diagnose the reticular stage which precedes the miliary. In such cases, radiography reveals massive hilar densities. In Boeck's sarcoidosis the tuberculin skin test is negative.

Among other disseminated lung lesions, dust-borne pulmonary infections (pneumoconioses) are of particular interest. The most important of them is silicosis, often encountered together with tuberculosis. Radiologically, it is seen as a multitude of disseminated minimal foci and in certain cases resembles tuberculosis, while in older patients similar pictures are observed in disseminated sclerosis. Quartz contamination at times gives pictures of sclerotic changes resembling the sclerotic forms of tuberculosis with hematogenous dissemination. A detailed anamnesis (occupational dust-contamination) is extremely

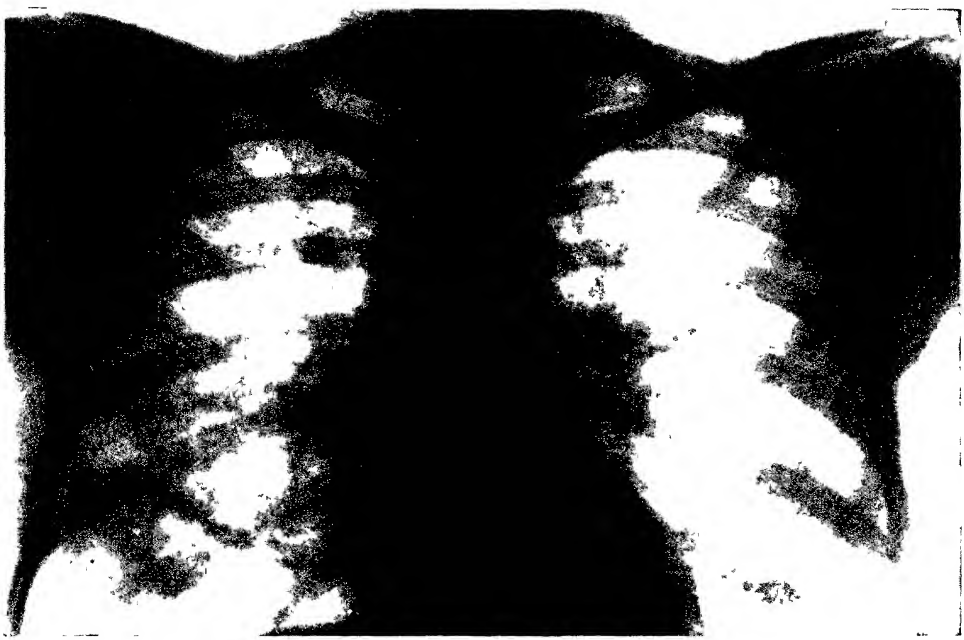


Fig. 54. Silicotuberculosis

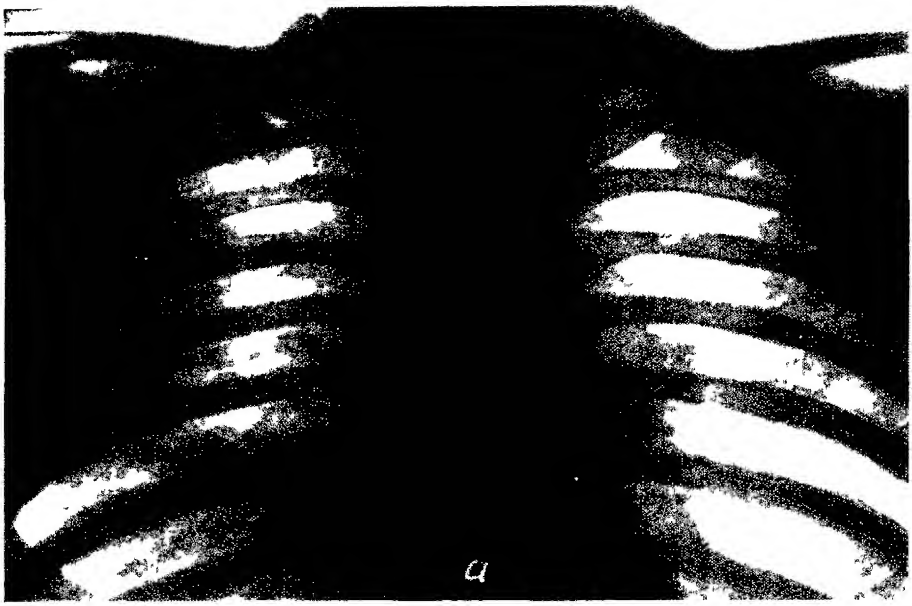


Fig. 55a. Eosinophil pneumonia (blood eosinophils 22 per cent)

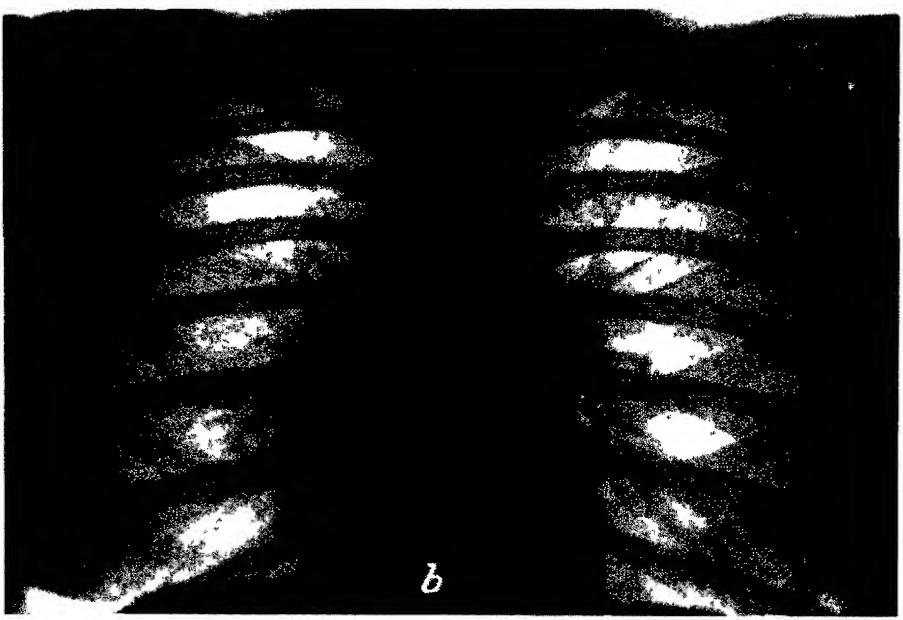


Fig 55b The same case 6 days later Complete resorption of pneumonic changes

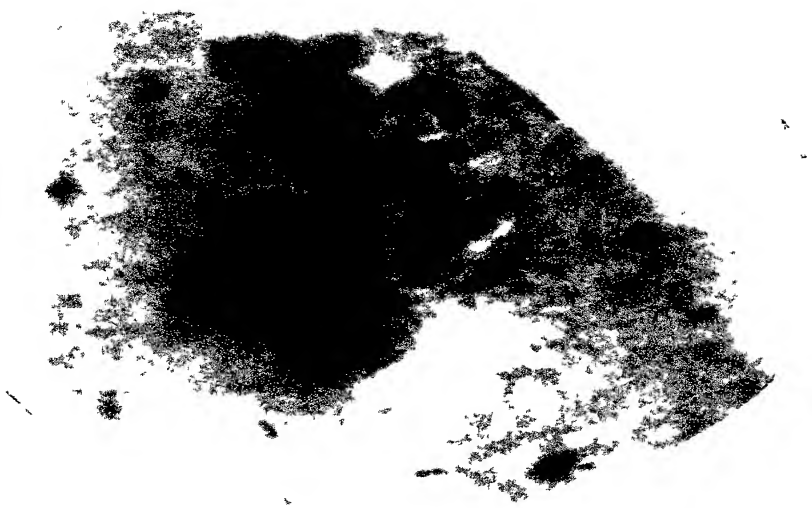


Fig 56 Cancer cells in the sputum (direct smear microscopy, F A Istomina)

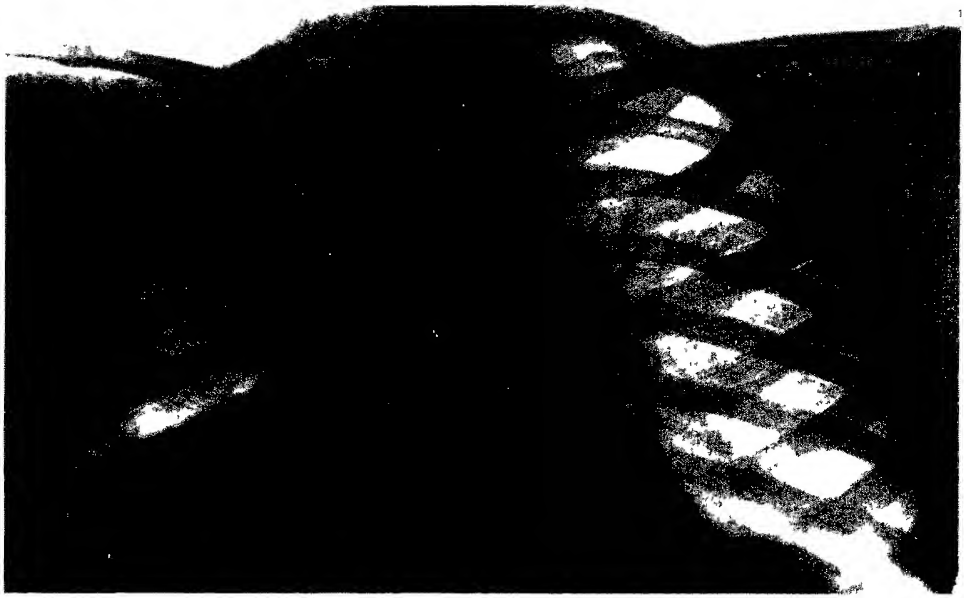


Fig 57 Massive lung consolidation with atelectasis (pneumocarcinoma)

important. Differential diagnosis in cases of combined silicosis and tuberculosis (Fig. 54) is essential, since prognosis in such cases is grave.

Lately, physicians have learned to distinguish certain rare forms of the disease, such as essential hemosiderosis, which is one of the manifestations of collagenosis, eosinophilic granuloma and certain others.

PARENCHYMAL THICKENING

The radiological picture in various cases of parenchymal thickening is connected with the anatomic nature of the changes and variations in its radiographic presentation.

Limited thickening appears in the form of soft densities and clearly outlined indurated or calcified foci of varying size—from a millet grain to a hazel nut and larger. Bigger circular densities (from 1 to 5 cm in diameter) appear with tuberculous infiltrations, i.e., foci of exudative inflammation, or with incapsulated foci of the type of tuberculomata, or, finally, with residual fibrocaseous changes. In the case of fibrocaseous changes, the contours of the density are precise, similar pictures being observed in peripheral bronchogenic pneumocarcinoma, hamartoma, and benign tumours like fibromata or cysts.

More extensive thickenings, involving one or several segments or a lobe, are observed in tuberculous and non-tuberculous pneumonia. In addition, one should not overlook the significance of atelectasis in lung pathology.

In differentiating minimal and, particularly, soft foci of tuberculous origin, one should carefully study the family history, bearing in mind the possibility of exposure and reinfection. The solution is prompted by follow-up and the speedy effect of antibacterial therapy. Indurated tuberculous foci are stable and inert; they are not amenable to chemotherapy and do not require it.

Of particular interest among the focal and pneumonic lesions in adults are so-called transient infiltrations, mostly with concomitant eosinophilia but without leukocytosis, which are referred to as Loeffler's syndrome, which proceeds as a fast-developing allergic reaction (Fig. *55, a* and *55,b*).

Such conditions, radiologically similar to tuberculous infiltrations, mostly proceed with minimal manifestations, subfebrile temperature and malaise, and are sometimes completely unnoticed by the patient. Stethacoustic findings are scarce, seldom including small-sized moist rales; in subpleural localisations, the sound of pleural friction is audible Usually, such infiltrations resolve in a matter of several days (within 2 weeks), without any radiographic traces, as distinct from conventional tuberculous lesions in which residual changes mostly remain even after clinical recovery (areas of sclerosis, incapsulation or induration). This is especially conspicuous under contemporary chemotherapy.

Differentiation between membraneous and caseous pneumonia is at first rather difficult. An acute onset with high temperature (39 to 40°C) with shooting pain in the thorax, crepitant rales in the lung and pronounced leukocytosis (20,000 to 30,000) is more characteristic of non-specific pneumonia. The answer is provided by the subsequent course—the refractoriness of tuberculous pneumonia in regard to penicillin and sulfonamides. Antituberculous drugs, although active, have a slower effect here than in other forms of pulmonary tuberculosis. In benign cases, they all reduce the pulmonary changes.

It is often most difficult to differentiate between tuberculosis and malignant neoplasmata, which has undoubtedly become more prevalent in recent years. The shadows of tuberculous infiltrates and blastomatous neoplasmata are closely similar, but the semiology of these diseases is nevertheless different. Pain and overpowering cough are more frequent in advanced forms of pneumocarcinoma. In a majority of cases they are accompanied by hemoptysis. In the more advanced cases of carcinoma, the number of red blood corpuscles diminishes. The E.S.R. almost invariably persists at high levels (30 to 50 and more mm per hour) in malignant neoplasmata. As regards the hemogram, a neutrophil shift to the left and monocytosis are mostly observed in tuberculosis; malignant neoplasm is predominantly accompanied by secondary anemia. In cancer, disintegration of the cavitary type is encountered more rarely but pneumonic superimposition may occur.

In certain bronchogenic forms of carcinoma (hilar localisations) modern bronchoscopy is a great diagnostic aid. On some occasions bronchography reveals a break in the bronchial shadows filled with contrast matter. The presence of mycobacteria in the sputum should always arouse suspicion, but it may often be sterilised by chemotherapy.

Cytoscopy of the sputum on direct smears and celloidin sections is an important diagnostic aid. Here the presence of atypical cellular elements with a considerable percentage of mitoses is pathognomonic for neoplasm. Attentive study will reveal them in great numbers (F. A. Istomina) (Fig. 56).

With enlarged and indurated lymph nodes, e.g., over the clavicle or in the axillary area, cytology of the punctate or biopsied sections may help to differentiate tuberculosis from such systemic conditions as lymphogranulomatosis or sarcoidosis. Indurations associated with the development of atelectasis may be short-lived, as, for instance, in obturative atelectasis and bronchial occlusion by viscous muca or a blood clot. After the removal of the latter, the atelectasis resolves spontaneously or by aspiration through the bronchus. A different picture appears when atelectasis sets in after compression of the bronchus by indurated tuberculous lymph nodes, as occasionally observed in children and adolescents, or when a neoplasm proliferates into the bronchial passageways (Fig. 57). Here compressive-obturatory complications are more difficult to remove.

Attention should also be paid to findings indicating the development of contractile bronchospastic atelectases. In certain cases, e.g., after cranial trauma, laminar atelectasis, i.e., atelectasis of neuroreflex origin, develops.

PARENCHYMAL SOFTENING. BRONCHIAL LESIONS

Diffuse softening of the pulmonary tissue occurs in various forms of pulmonary emphysema, both vicarious and compensatory, e.g., in the lung contralateral to the one under operation. Here we shall deal with the differentiation of pulmonary cavities. Apart from the characteristic course of the disease, tuberculous cavities are confirmed by the presence of mycobacteria and elastic fibres in the sputum. With negative sputum, various possibilities should be considered. Cavitary forms of bronchogenic pulmonary carcinoma and numerous instances of cavities of bronchiectatic origin have been recorded. In the latter case, the chronic and often permanent course of the disease with periodically arising interstitial pneumonia and abundant expectoration typical of pyosclerosis are factors assisting differentiation. Cavities develop acutely where there are pulmonary abscesses, often with the characteristic sloughing (expectoration of sputum by the mouthful) of large quantities of purulent sputum and, in febrile conditions, with chills. Cavities may also arise in actinomycosis and other mycetogenic diseases, e.g., candidamycosis.

Here careful sputum study, revealing mycelium and druses in the former case, and *candida albicans* in the latter, help to establish the diagnosis, with due account, of course, for the serologic reactions.

Cystous lesions may be filled, as, for instance, are dermoid cysts. There are also the so-called air cysts which are spherical, thin-walled and sometimes solitary, from 6 to 8 cm in diameter, or occurring in clusters as, e.g., in a congenital cystous lung. Occasionally, bronchiectasis may resemble air cysts, especially in the dry stage.

One should also make allowance for the possible emergence of bullous-type cavities resembling bullous emphysema and presenting lesions remaining after the healing of the walls of a tuberculous cavity. In recent years such cases have been recorded after continued chemotherapy for cavernous tuberculosis.

DISEASES INVOLVING THE INTRATHORACIC LYMPH NODES

Mediastinal Lesions

Tumor mediastini proper is a symptom observed in etiologically different mediastinal lesions. Differentiation is often concerned with a tumour-like enlargement of the lymph nodes—unilateral in tuberculosis and lymphogranulomatosis and bilateral in lymphosarcoma. Besides, one should not overlook aortic aneurisms, esophageal

diverticules, etc. Here, careful clinical and radiographic examination, especially multiaxial radioscopy, are of practical help.

Inflammatory processes in the mediastinum—mediastinites—may be linked with lesions of the lymph nodes, trachea, bronchi, esophagus, etc.

Boeck's Disease

In this peculiar condition described by Boeck in 1899 and by Shauman in 1914, pulmonary lesions are sometimes accompanied by lesions of the skin, mucosa, lymph nodes, spleen, liver, lungs, nervous system, bone marrow, eyes, etc. The histologic picture in biopsy is very typical, presenting nodules of epithelioid cells with a thin girdle of lymphocytes and random giant cells, which may, in some cases, be totally absent. The lesion resembles a tubercle, but there is no sign of any elements of exudative inflammation or caseation. The process involves the reticuloendothelial system.

The disease undergoes three stages:

I—lesion of the hilar lymph nodes;

II—reticular, miliary or mixed;

III—confluent and fibrous.

Lesions of the hilar lymph nodes are usually bilateral, in contrast to lymphogranulomatosis with its mostly unilateral involvement of the hilar nodes.

Involvement of the pneumoparenchyma indicates progression, but generally prognosis is relatively benign, especially in the initial stage. The course is prolonged. Etiology has not yet been established. Some indications point to the probability of a tuberculous etiology. Usually a tuberculin test is negative, though not always. Another characteristic feature is the benign effect of hormone therapy (cortisone, prednisolone, etc.).

Involvement of the hilar nodes is likewise observed in tuberculosis, especially in initial stages.

A further well-known condition is lymphosarcoma. In bronchogenic pulmonary carcinoma, as stated earlier, the hilar nodes are also involved.

In relation to differentiation between tuberculous and non-tuberculous diseases, especially malignant neoplasms, it is necessary to note the growing frequency of such neoplasms, which should be borne in mind to avoid diagnostic errors.

PARASITIC DISEASES

Diagnostic difficulties often arise in differentiating parasitic pulmonary diseases. In hydatid cysts, which increase quite rapidly, the Cazzoni's test is usually positive. Hemoptysis and subfebrile temperature sometimes occur initially. The radiological picture in hydatid disease is characteristic but, of course, not pathognomonic.

One should also consider the possible development of pneumonia in cases of migrations of ascarid larvae. Family epidemics of this type of pneumonia have been recorded, accompanied by other allergic manifestations, such as urticaria and eosinophilia. The feces must be examined for eggs of helminths.

Radiological pictures have recently been observed resembling tuberculous infiltrations, reflecting minimal cavities caused by *distomum pulmonale.* In such cases the sputum reveals the characteristic larvae of the parasite. Finally, one must note another important factor. Today, with the changes in the course of tuberculosis brought about by chemotherapy, which has considerably increased the life expectancy even in grave cases, combinations of tuberculous and non-tuberculous diseases, e.g., tuberculosis and cancer, are more frequently encountered.

These considerations do not, of course, exhaust the possibilities offered by differential diagnosis in pulmonary diseases, but are intended to draw attention to the lines along which examination, clinical and otherwise, will facilitate the correct solution of diagnostic problems in pulmonary pathology.

CHAPTER X

EXTRAPULMONARY TUBERCULOSIS

TUBERCULOSIS OF THE LARYNX

Until recently, tuberculosis of the larynx represented the tragic culmination of pulmonary consumption, mostly accompanying pulmonary tuberculosis. Laryngeal lesions used to be observed in 20 to 25 per cent of cases, whereas today, thanks to chemotherapy, this condition occurs only in 4.1 per cent (Calseyde). Invasion of the laryngeal mucosa occurs sputogenously, but in some cases the hematogenous route is also beyond doubt. In clinical practice, following A. N. Voznesensky, according to course and form, we distinguish infiltrative, productive and ulcerous-exudative laryngeal tuberculosis The sites of predilection are the true and false vocal cords, posterior wall and epiglottis (Fig. 58). In severe cases, perichondritis occurs.

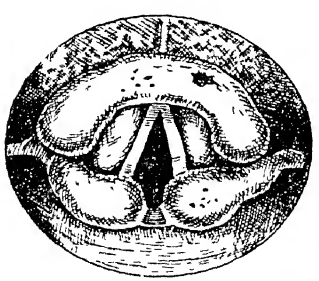


Fig 58 Infiltrative-ulcerous tuberculosis of the larynx

The course may vary depending on the general condition of the patient and the incidence of lesions in other organs, particularly the lungs, but mostly it is chronic. Ulcerative forms develop in cases of epithelial necrosis, with the growth of granulation tissue. At times, infiltration is so extensive that symptoms of laryngeal stenosis develop, but today this is very rare.

Difficulties of differentiation occasionally arise in diagnosing laryngeal cancer, biopsy sometimes giving the correct analysis.

Lesions of the larynx should be identified as soon as possible, i e , in their initial appearance. Since the disease may at first develop without symptoms, prophylactic inspection of the larynx is obligatory for all patients. Sparing treatment (silence) with rational supportive measures now takes less time, combined chemotherapy (phthivazid, streptomycin and P.A.S) in most cases leading to recovery.

TUBERCULOSIS OF THE TRACHEA AND BRONCHI

Isolated bronchial tuberculosis occurs comparatively seldom, the lesion mostly accompanying tuberculosis of the lungs or intrathoracic lymph nodes. The bronchi may also be affected as a result of hema-

togenous dissemination. In fibrocavernous tuberculosis, there is in fact a bronchocavernous syndrome in which the process mostly involves the draining bronchus (A. A. Lapina).

Today we have the means for diagnosing the broncho-fistulous forms of tuberculosis (K. A. Deli, F. Shwartz et al.), when the lymph nodes with caseous necrotic foci adjoining the bronchus adhere to its wall and rupture into its lumen, which leads to the formation of a fistulous passageway similar to the process observed in the softening of cervical lymphadenitis or in the formation of a skin fistula. Small fistulae heal after several weeks or months, leaving small scars. In more severe cases, the rupture is more extensive, producing a crater-like ulcer in which bronchoscopy may even reveal the underlying bronchial cartilage. Isolated bronchial tuberculosis may take an infiltrative-ulcerous form (Fig. 59).

As stated earlier, bronchial lesions are mostly subsidiary to pulmonary tuberculosis, especially in its cavitary stage There are, however, cases when a bronchial lesion is followed by the development of pulmonary tuberculosis, as observed in certain cases with broncho-fistulous forms.

In cavernous cases, the bronchial lesion may probably be the result of permanent contact between the mucosa and the purulent cavital content, forming, as it were, a continuation of the cavity In such cases there is usually an abundance of tubercle bacilli Often, there are infiltrations of the bronchial mucosa and, later, ulcerations with undermined edges. Occasionally, the process involves destruction of the cartilage.

Persistent cough is the most conspicuous individual symptom of tracheal and bronchial lesions Any signs of bronchospastic and/or bronchial catarrh of an allergic nature, linked with the hypersensitation of bronchial mucosa in pulmonary tuberculosis, should also be noted. According to I P. Garaix, the lesion may take any of the following forms: bronchoscopical limited ulceration (48 per cent), ulceration with stenosis (19 per cent), stenosis (23 per cent), proliferative perforation, growth and tuberculomata (10 per cent)

The chemotherapeutical healing of more or less extensive bronchial lesions may be followed by bronchial stenosis which is well demonstrable bronchographically.

Treatment and Prognosis. Limited lesions of the trachea and bronchi respond readily to combined chemotherapy, particularly when streptomycin is used. Local treatment comprises cleansing the ulceration with a cottonwool swab, followed by the application of *Sol. Argenti nitrici* (30 to 50 per cent) or *Ac. trichloracetici.* Quartz irradiation through a bronchoscope is administered for 3 minutes. Bronchocavernous forms are successfully treated by aerosol therapy (streptomycin, saluzid, tubazid, larusan, etc), such spasmolytics as atropine, platyphylline or ephedrine being added to the aerosol solution On a number of occasions good results are obtained from in-

tratracheally administered drugs under cover of conventional combined chemotherapy.

Stenosis of the major bronchi may be eliminated only surgically.

TUBERCULOSIS OF THE ABDOMINAL ORGANS

Gastric tuberculosis is a rare occurence. In pulmonary tuberculosis such localisations are encountered in no more than 0.6 to 2 1 per cent of all autopsies. Intestinal tuberculosis, which causes grave complications in patients with pulmonary tuberculosis, was until recently a very common occurence (in 57.6 per cent of all cases, according to the author's own sectional findings of 1947). With the introduction of streptomycin, intestinal tuberculosis occurs considerably less often —according to the sectional findings of N. P. Krylova (1957), only in 23.7 per cent of cases. As mentioned earlier, the Lubeck disaster proved the possibility of the development of an enteral primary complex.

Intestinal affliction of the primary complex type is probably accompanied by changes in the mesenteric lymph nodes. Intestinal lesions may occur in acute generalised forms of tuberculosis, but the possibility of such lesions in hematogenous dissemination cannot be ignored.

One must note that in pulmonary tuberculosis toxicemia and specific sensitation may often cause non-specific colitis of a spastic nature which is probably conducive to further progression.

Post-primary intestinal tuberculosis occurs chiefly in the following forms:

1. An infiltrative-ulcerous lesion of the small and large intestine;
2. Hypertrophic ileocecal tuberculosis;
3. As the result of a progressive tuberculous primary lesion of the mesenteric lymph nodes.

Ulcerous intestinal tuberculosis is often accompanied by fermentative or purulent dyspepsia. These symptoms, however, mostly occur in the terminal stages The onset is often marked by constipation with spastic manifestations.

Patient A V., female, age 29, had pleurisy with effusion in the left lung in 1948 A year later, focal pulmonary tuberculosis revealed, mycobacteria non-apparent. Simultaneously, pains developed in the umbilical area, accompanied by nausea and constipation. Nutrition reduced. Tongue moist, uncoated Stomach of normal outline with moderate swelling in the right iliac area. Cecum and ascending colon painful at palpation. Blood picture Hb 60 per cent, leukocytes 5,600, E S R 10 mm per hour. Gastric juice. overall acidity 5, tied and untied hydrochloric acid 0 (thick tube). Coprogram· feces amorphous, with muca; organic acids 21 units, ammonia 8.2 units

Gastrointestinal radiology, March 19, 1953. stomach free of barium after four hours; iliac loops of uneven calibre with serrated contours contrast streaks and mottled mucosa on the wall of the ascending colon at the hepatic sinus and the proximal part of the transverse colon, tight filling with deep haustra in the medial part of the transverse colon (Fig. 60, *a*). Diagnosis· chronic disseminated pulmonary tuberculosis, achylia, fermento-purulent dyspepsia, ulcerous tuberculosis of the ileum, cecum and ascending colon.

Fig. 59. Infiltration with fistula in bronchus (from monograph by Schmidt)

Fig 60a Spastic filling defect of cecum, ascending colon and proximal part of transverse colon

Fig 60b The same case after treatment with streptomycin and P A S Tight filling of cecum and ascending colon

The patient received 60 g streptomycin and 500 g P.A S At repeated examination January 1954, no complaints of gastrointestinal disturbances Gained 5 kg Temperature remained normal Abdominal pains absent, stool well formed, daily. Pulmonary focal densities resorbing Gastric tests show achylia as before Coprogram feces well-shaped, with muca, organic acids 18 units, ammonia 4 8 units.

Post-treatment intestinal radioscopy revealed complete absence of the spastic filling defect, iliac loop segments smooth-walled, large intestine began filling after four and a half hours, tight filling of cecum and ascending colon noted after 7 hours (Fig 60, *b*)

Conclusion disseminated pulmonary tuberculosis with ulcerous intestinal lesion; showed considerable improvement in pulmonary and intestinal condition after course of antibacterial therapy

Pictures of hypertrophic ileocecal tuberculosis, with the radiologically characteristic symptoms of the filling defect described by Stirling in 1911, are a comparatively rare phenomenon.

In all cases of intestinal tuberculosis, adequate radiology with barium introduced per os or, in some cases, per klysmam is of major importance, yet abdominal palpation after V. P. Obraztsov helping to localise the lesion and also useful in screening should not be neglected.

In recent years tuberculous mesadenitis has been diagnosed far more often than justified. Such a syndrome, however, with acute or chronic pain, intestinal diskinesia, subfebrile temperature and refractory wasting, may, of course, be encountered in children, adolescents and young people. Well-developed radiograms often reveal clusters of partly calcified lymph nodes on both sides of the spinal column. Occasionally, such clusters are localised at the level of McBurney's point and simulate appendicitis attacks.

Thorough hematological study is extremely helpful to diagnosis as are graduated tuberculin tests, which in such cases are sharply positive, particularly in adolescents and children. Hygienic and dietary measures and administration of phthivazid with P.A S., have a beneficial effect on cases with mesadenitis. Occasionally, quartz irradiation may prove useful, provided there are no active pulmonary changes.

Isolated lesions of the liver and spleen are extremely rare. Lesions of these organs mostly develop in generalised tuberculosis.

TUBERCULOUS PERITONITIS

We shall not deal here with the tubercular peritoneal seeding observed in miliary tuberculosis. The forms most frequently involving the peritoneum are: (1) ulcerous intestinal tuberculosis; (2) tuberculous mesadenitis; (3) female genital tuberculosis (salpingitis).

Exudative peritonitis is distinguished from its dry or plastic modification, although there is almost always an exudative reaction in the initial stages. Later, depending on the allergic stage, there is a preponderance either of exudation or plastic inflammation. Initially, diagnosis may be extremely difficult, and only careful anamnesis and analysis with due account of family background, past diseases, primary

infection, intensity of tuberculin reaction offer grounds for suspecting peritonitis. Of course, in cases when exudate is less abundant, abdominal percussion in the knee-elbow position helps to confirm the diagnosis. Examination of senile patients should always make allowance for carcinoma, especially if specific lesions of other organs, primarily pulmonary tuberculosis, are not present.

UROGENITAL TUBERCULOSIS

Urogenital tuberculosis is usually the result of hematogenous metastasis. This basically refers to renal tuberculosis. Tuberculosis of the urinary bladder is always secondary.

As indicated earlier, renal tuberculosis may arise owing to hematogenous dissemination, e.g., in miliary tuberculosis, or from hematogenous metastasis spreading and developing locally. Initially, the minimal tuberculous focus breaks into the urinary tubule, which is followed by the emergence of a small ulcerous lesion in the renal sinus. This condition is described as an early form of cavitary renal tuberculosis.

Renal tuberculosis, in which the pronounced lesion is most frequently localised in one kidney, proceeds chronically, sometimes continuously, without symptoms. This explains the still frequent diagnostic errors in initial renal lesions even with the presence of pulmonary tuberculosis.

Some authors draw attention to the albuminuria accompanied by the absence of formed elements in the urine, which precedes more pronounced symptomatology. The incidence of pyuria always demands attention and thorough examination. The symptoms of chronic renal tuberculosis include primarily dysuria with nycturia and pollakiuria. Urination becomes more frequent especially when accompanied with urinary bladder disorders resulting in considerable decrease of the volume of urination which becomes painful and is followed by tenesma. At times, the disease is symptomatised by primary hematuria or a colic syndrome of the kidney.

The presence of tubercle bacilli in sterile catheterised urine gives definitive confirmation of the diagnosis. In renal tuberculosis, the urine usually contains no other microorganisms.

Thus, the presence of pyuria and tubercle bacilli are essential for diagnosis. Of course, as in other renal afflications, functional examination and, primarily, catheterisation of the ureters is imperative. The major importance of radiology with the use of contrast substances in manifest forms of the disease must also be noted, employing, first of all, such methods as descending pyelography (introduction of contrast matter at catheterisation of the ureters).

In cavernous lesions of the kidneys, radiography with the use of contrast media gives conclusive results (Fig. 61).

Secondary lesions of the bladder may be associated with a kidney lesion. In addition, tuberculous epididymitis and prostatic lesions may also indicate tuberculosis of the bladder accompanied by severe

dysuric manifestations It is important to note that in females simultaneous involvement of the urinary and genital organs occurs extremely seldom, whereas in males it is apparent in two-thirds of all cases.

Differential diagnosis of renal tuberculosis mostly has to take into account nephrolithiases and tumours (the latter mostly with considerable hematuria).

Treatment commences with a combination of streptomycin and phthivazid. Nowadays an afflicted kidney is resected under cover of chemotherapy, if one kidney is destroyed and the other functionally intact.

Patient A, female, 24 years of age, had miliary pulmonary tuberculosis and tuberculous meningitis when 20, for which she took a 10-months clinical course of streptomycin Discharged after clinical recovery, resumed work Four years later (1955), pains developed in the lumbar area and lower parts of the abdomen with frequent and painful urination Urinalysis revealed profuse leukocytes, urine cultivation showing the presence of tubercle bacilli. Diagnosis. tuberculosis of the right kidney After antibacterial chemotherapy (50 g streptomycin and 48 g phthivazid) was discharged with improvement In 1959, influenza was followed by exacerbation Hospitalised with complaints of increased fatigue, lumbar pains

Objectively, no abnormal physical deviations in the lungs Radiology showed groups of indurated minimal foci in the apical areas of both lungs

Blood picture er 3,560,000, leuk 6,900, eos 2 per cent, band cells 6 per cent, segmented cells 56 per cent, lymph 30 per cent, mon. 5 per cent, E S R 13 mm per hour Urine reaction acid, sp gr 1018, protein 0 3‰, leukocytes up to 25 at one view, occasionally conglomerated, *Mycobacterium tuberculosis* and other flora bacterioscopically absent Urine catheterised from the left kidney contained pus (leukocytes in clusters at many views); on the 30th day a growth of tubercle bacilli was observed, urine from the right kidney negative, leukocytes up to 20 at a view.

Retrograde pyelography revealed changes (softening) about the medial and anterior calyces at the right (Fig 62). Genitals showed no deviation from the normal.

Diagnosis focal pulmonary tuberculosis in the stage of induration, tuberculosis of the right and left kidneys

Treated clinically for 3 months with antibacterial drugs (1 g streptomycin, 1 g phthivazid daily), which gave positive results.

Conclusion a clinical example of the development of renal tuberculosis (first in right kidney, then in left) owing to hematogenous generalisation; a history of miliary tuberculosis and tuberculous meningitis.

AMYLOID NEPHROSIS

Amyloid nephrosis, like amyloidosis of other organs, is a local manifestation of general amyloidosis (hepatic, splenic or intestinal) implying a grave disturbance of protein metabolism with concomitant dysproteinemia, i.e., pathological disturbance of the blood protein ratio.

Amyloidosis, in particular amyloidosis of the kidneys, is caused by perennial, chronically proceeding tuberculous lesions of the lungs, especially fibrocavernous tuberculosis, tuberculous and mixed purulent pleurisies and fistulous tuberculosis of the bones and joints. There are, however, cases when amyloidosis arises despite the limited nature of the principal tuberculous lesion.

Amyloid is first deposited in the glomerules, then in the basal membranes of the tubules. The renal function is usually sharply im-

paired. The urine is of low specific gravity and is rich in protein while poor in formed elements. If there is a concomitant lesion of the intestine accompanied by follicular colitis, the patient complains of diarrhea. In severe cases, as in lipoid nephroses, edema and ascites develop. The pure forms of amyloid nephrosis are characterised by an absence of eye-ground changes and of arterial hypertension. If amyloid nephrosis is accompanied by changes of the type of kidney retraction, the result is all the symptoms of renal insufficiency, the patient ultimately dying of uremia.

Treatment in amyloid nephrosis is symptomatic. In this primary stage, attempts should be made to eliminate the initial cause, i e , the purulent pleural lesion.

In recent years, partly on the basis of experimental works, some authors (A. I. Abrikosov) have inclined to the view that minimal changes in amyloid nephrosis are reversible.

THE ENDOCRINE SYSTEM AND TUBERCULOSIS

Functional disturbances of the endocrine system in tuberculosis may be associated, first, with the effects of intoxication and, second, directly with tuberculous lesions of the respective organs—the adrenopituitary system, adrenals, genital glands, etc. In the former case, the disturbances disappear together with the cessation of toxicemia, while in the second, the functional disorders depend on the nature of the glandular lesion.

Tuberculosis of the adrenals occupies a place apart among the diseases of this group. Mostly, there is a bilateral lesion in which the process (caseous necrosis) involves not only the cortex, but the medulla.

One of the more pronounced forms of the lesion is known as Addison's disease. The most conspicuous symptom here is emaciation, acute adynamia and hypotension. Hypoglycemia with marked insulin sensitivity and a sharp reduction of glycogen in the liver and muscles are observed. The residual nitrogen content of the blood increases, which is accompanied by blood congestion, leukopenia and lymphocytosis. There is a considerable drop in blood sodium and an increase of blood potassium. General dehydration is also observed A notable feature is the changed pigmentation of the cutanea, the skin folds under the armpits, in the groins and at points of contact with the clothing, as well as the pigmentation of the mucous membranes on the lips and cheeks. This pigmental disturbance is the result of excessive secretion of melanine which is apparently related to an insufficiency of vitamin C in the adrenals destroyed by caseous necrosis and the lack of the adrenal regulation of pigment metabolism, a function similarly associated with the pituitary.

In its advanced form, the disease is absolutely incurable. A certain degree of compensation is obtained by systematic administration of desoxycorticosterone acetate (DOCSA), vitamin C and noradrenalin.

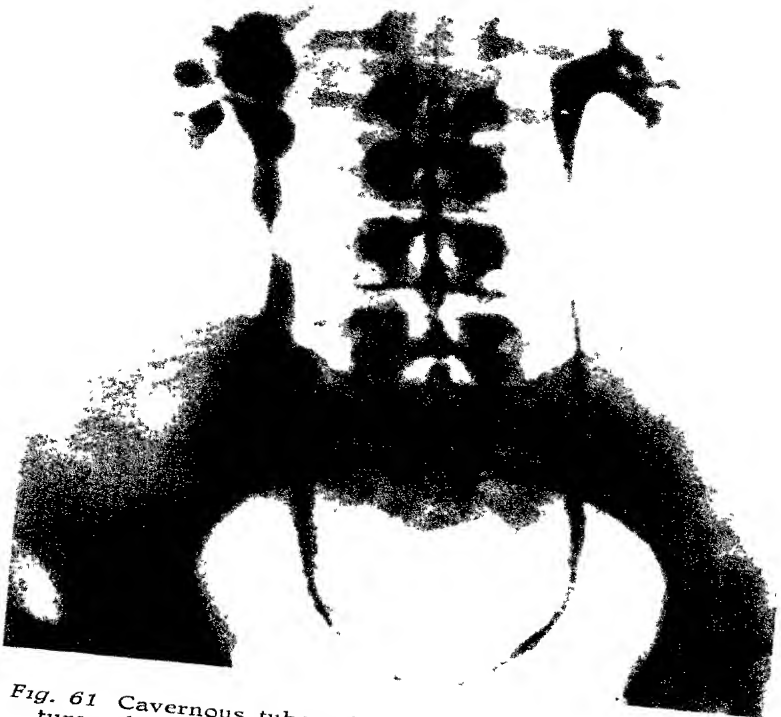


Fig. 61 Cavernous tuberculosis of the right kidney Structure of ureter Left kidney unaffected (pyelogram)

Fig 62. Pyelogram of patient A. Tuberculous lesion of the left kidney

As regards other changes in the endocrine organs, functional disturbances on the part of the thyroid are another lesion of this type. Hyperfunction of the thyroid is observed in a number of cases as a result of tuberculous intoxication. Such disorders are accompanied by an increase of basal metabolism. Commonly, they are not sharply pronounced and disappear when intoxication ceases.

CHAPTER XI

PREVENTION AND CONTROL

EPIDEMIOLOGY

The epidemiology of tuberculosis is determined by the features of the pathogen, the routes of infection, the body reaction, and the socio-economic and living conditions of the people. For thousands of years, tuberculosis afflicted wide sections of the population all over the world, its incidence depending on the living and working conditions of a particular society. Hence, tuberculosis is classified among social diseases.

Because there was no systematic notification of cases, estimates of its frequency were based on the findings of special selective surveys which were undertaken sporadically and based largely on the TB death rate.

In pre-revolutionary Russia tuberculosis morbidity was extremely high among both rural and urban population. Local doctors reported an especially high morbidity in rural areas. Some idea of the morbidity in urban areas may be obtained from the diagram (Fig. 63) demonstrating schematically tuberculous mortality in Moscow for the years 1878-1956.

As can be seen from the diagram, the TB death rate in Moscow has fallen considerably. The figures illustrating this decline are striking. During the forty years preceding the Great October Socialist Revolution, the mortality rate in Moscow decreased by less than half. In the subsequent 35 years, when public health became a matter of government concern, when the Communist Party and the Soviet Government took comprehensive measures to improve living standards, and when the fight against tuberculosis assumed a definite purpose and orientation, the figure fell more than 900 per cent, although the period includes two world wars which brought an increase in tuberculosis morbidity, which is also vividly reflected in the diagram. It is similarly important to note that, owing to the special measures taken by the Government, peak mortality from tuberculosis after the Great Patriotic War was considerably lower than after the First World War.

The compulsory notification of all active cases which made it possible to evaluate its epidemiology directly, and not on the basis of

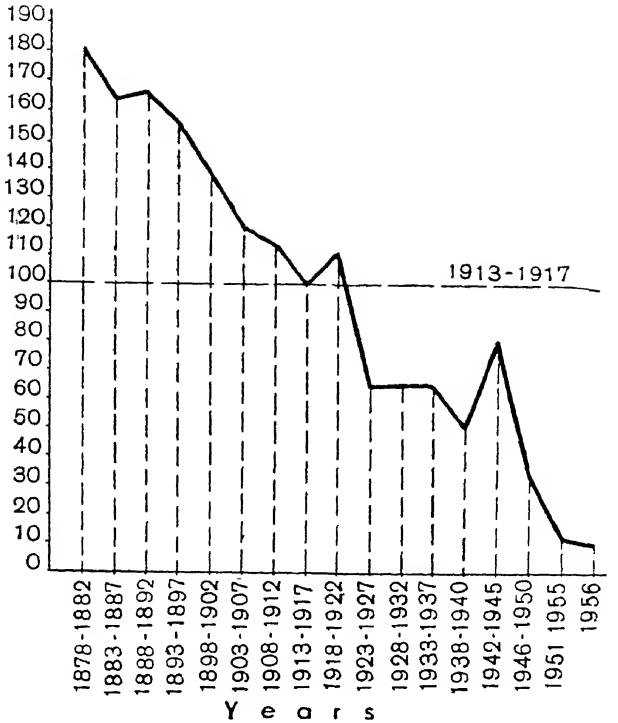


Fig 63 Annual tuberculosis mortality in Moscow (per cent, 1913-1917=100) 1878-1956 (after I. D. Zaslavsky)

mortality was of major importance for the adequate organisation of tuberculosis control in the U.S.S.R. As a consequence, we possess information on total morbidity as well as on infectivity, i.e., the number of fresh cases each year.

Analysis of this data shows a systematic and consistent decrease in tuberculosis morbidity. Between 1950 and 1955, the tuberculosis sick rate in cities of the U.S.S.R., according to A. I. Lapina, decreased by 34.7 per cent, the rate of respiratory tuberculosis by 35.2 per cent, and that of open forms by 46.1 per cent. In subsequent years there was a further tendency towards decrease. Essential changes are obvious in the pattern of fresh cases (Table 1).

As the table shows, during the last 11 years the rate of nodular and infiltrative tuberculosis among fresh cases has become between 2 and 2.5 times, that of dissemination 4 times and of fibrocavernous tuberculosis 12 times less. The rate of cases involving disintegration has fallen by 80 per cent. There is a considerably lower incidence of tuberculous meningitis; cases of miliary tuberculosis and caseous pneumonia are extremely rare.

The number of fresh cases is diminishing every year. In this connection, it is interesting to note the various factors affecting the

Table 1

Comparative Data on Fresh Adult Cases of Tuberculosis Revealed in Moscow

(per cent, 1947=100)

Clinical Forms and Stages	1947	1953	1956	1957	1958
Nodular	100	86 6	59 8	57 2	51 6
Infiltrative	100	65 4	47 4	42 6	44 0
Disseminated	100	49.8	28 0	25 5	24 5
Fibrocavernous	100	18 8	9 9	7 7	8 1
Disintegration	100	33 8	21 1	19 0	20 0

decrease in the morbidity for different forms. If prior to 1948 the frequency of lethal cases was many times greater than that of recovery, in the following years there was a predominance of recoveries. The rate of recoveries in active adult cases in Moscow for 1940-1948 comprised 4 to 6 per cent, in subsequent years reaching 12 to 14 per cent. The frequency of recovery in children was 25 to 30 per cent It is important to note that in recent years the number of recoveries has exceeded that of fresh cases, which accounts for the reduction of notified cases. Hence, at the present stage, morbidity and recovery figures are the two indices demonstrating the efficiency of our anti-tuberculosis control measures. In other words, tuberculosis control is effected along the lines of preventing morbidity and conducting effective therapy in existing cases.

The social factor is of paramount importance in preventing morbidity. In this respect, the socialist changes carried out in the Soviet Union have created exceptionally favourable conditions. Suffice it to mention the elimination of unemployment, socialist labour legislation, the establishment of good working conditions, the labour protection measures in industrial enterprises, the continuous growth of living standards, the increase in housing construction which has developed at an unprecedented rate in recent years and the growth of cultural and general welfare standards, etc. In these circumstances, special measures conducted on a large scale taking into account the infectional etiology of tuberculosis, assume additional significance.

As stated earlier, the basic route of infection in tuberculosis is the aerogenic (through droplets and dust). The greatest hazard as far as infection is concerned is the sputum of bacillary tuberculous patients, which contains large quantities of tubercle bacilli. Although the other secretes (feces, urine, etc) also contain mycobacteria, they are seldom transferred into the air via dust, and hence are a much smaller epidemiological hazard. Nevertheless, disinfectionary measures should include sterilisation of all excreta.

Because the secretes of bacillary patients (chiefly sputum) fall in suspended or dry form on the surrounding domestic utensils and other objects, not only the bacillary patient himself, but the whole house and everything within it become a potential source of infection. Tuberculous infection may also occur through contact, or be contracted from animals. Mycobacteria of the bovine type, differing from the human, are often revealed in patients, especially children. Parenteral invasion has been proved possible in childhood. In actual fact, the main source of infection from animals is raw milk, tuberculosis of the udder being quite widespread among cows. On big farms, all the milk is collected in common vessels, and consequently the presence of one or two tuberculous cows in a herd is sufficient for the entire milk to become infected.

Direct invasion through the skin, although proved theoretically, occurs comparatively rarely in practice. Finally, we must re-emphasise the epidemiologically essential fact that invasion of the human body by tubercle bacilli merely implies infection, the development of the disease proper directly depending on the individual's general state—the immuno-biological balance of forces, resistance, living and working conditions, and other factors.

All this determines the basic targets and directions of morbidity prevention, which includes measures of sanitary and specific prophylaxis.

SANITARY PROPHYLAXIS

General Preventive Measures

The general preventive measures include:

1. *Universal physical training, from childhood onwards.* In children's institutions and in the family, at elementary, secondary and professional schools of all grades, constant attention should be paid to the physical education of children, adolescents and teenagers, which should also be a matter of concern at industrial enterprises. The possibilities offered in this respect by the entire socialist system of government and administration are extremely great. Physical culture, which has assumed a mass scale in the U.S.S.R., fosters the all-round and balanced development, physical and mental, of the human personality, strengthening resistance to infection.

2. *Provision of normal housing conditions conforming with hygienic requirements.* The importance of adequate housing for the prevention of tuberculosis cannot be overemphasised.

3. *Sanitary propaganda and education* is one of the basic means of prevention. Fundamental knowledge of the nature of the pathogen, the routes of infection, conditions of exposure, and the principles of individual and social prophylaxis should be made available in popular form to all sections of the population. There are many ways and means whereby sanitary education may be carried out, including talks with

patients, lectures to factory and office employees and farm workers, high-quality exhibitions and visual displays at medical institutions and propaganda through the local press and wall-newspapers, radio, television and films, etc This extensive propaganda should be carried out not only to spread the knowledge of specific precautionary measures against tuberculous infection, but should give advice on the behaviour of tuberculosis patients, allaying the exaggerated fear of tuberculosis and encounter with tuberculous cases (phthisiofobia).

4 *Protection of the entire population, children's institutions in particular, against the introduction of tuberculous infection.* Soviet legislation stipulates general health examinations of new employees and subsequent systematic health control of all employees Such control is carried out at children's institutions (nurseries, kindergartens, schools), establishments engaged in the production, processing and sale of food (cafeterias, canteens, kiosks, shops, bakeries, etc.), as well as communal establishments (hairdressers', civil transport, public baths, laundries, etc.), with the aim of preventing contact with tuberculous cases and their excreta.

Workers in antituberculosis institutions (dispensaries, hospitals, sanatoria), who have close contact with the tuberculous patients under their care, form a special category, being more exposed to infection than anybody else. Special regulations have been drawn up in the U.S.S.R. to safeguard the health of workers in antituberculosis institutions, laying down rules of employment, hygienic living and working conditions and measures of sanitation and disinfection. The observance of these regulations offers a considerable safeguard against the spread of infection among such employees.

5 *Mass population surveys for the prompt and total detection of tuberculous cases.* Annual mass surveys with compulsory X-ray examination are conducted among: (a) staff personnel and children at children's medical institutions; (b) personnel at general medical and prophylactic institutions and maternity homes; (c) school personnel and pupils, adolescents up to the age of 18 employed at state-owned and co-operative industrial enterprises; (d) office and factory workers occupationally exposed to dangerous working conditions and high temperatures; (e) public transport conductors, (f) people working in food-processing enterprises, warehouses, and food shops; (g) hairdressers; (h) university students In recent years a growing number of mass surveys have been conducted with the use of fluorography among office and factory employees at industrial and other enterprises, as well as extramural patients and the urban population The immediate task today is to conduct regular mass surveys of the entire population to detect all cases of tuberculosis which, as stated earlier, often proceed with no obvious symptoms. The familiarisation of general practitioners and especially therapeutists and pediatrists with the symptomatology and differential diagnosis of the initial forms of tuberculosis is tremendously important for early casefinding.

6. *Hospitalisation of tuberculous patients.* The prophylactic importance of hospitalisation lies in the fact that it affords the most favourable conditions for the treatment of tuberculous cases, thereby safeguarding the general population against exposure.

Domiciliary Prevention

Measures of individual sanitary prophylaxis, which are no less important than those enumerated, are aimed directly at creating healthy conditions in centres of tuberculous infection, i.e., dwellings with open cases of tuberculosis excreting tubercle bacilli. In the first place, patients must be instructed on the rules of individual hygiene in order to safeguard commensals. Much depends here on the patient's selfdiscipline. Such elementary habits as the use of separate towels, handkerchiefs, utensils, coughing discipline, the need to expectorate into special portable or stationary spittoons are of great importance for safeguarding the health of other people. The bacillary patient should have a separate room, the furniture of which should be easily cleansed and disinfected. In cases when a separate room is unavailable, a screen should be used to segregate the part of the room containing the patient's bed and personal furniture.

The patient should have a separate bed, at least half a metre from the wall and 1.5 to 2 metres away from other beds, if no screen is available. Crockery used by the patient should be kept and washed separately. His dirty linen should be kept in a special bag and washed separately from that of the other members of the family. His clothes should be kept on a special rack.

The basic measures of sanitary prophylaxis in a centre of infection include routine and terminal disinfection. Routine disinfection comprises daily sterilisation of the bacillary patient's excreta and objects liable to harbour mycobacteria. The home should always be wet-cleaned, wiping the floors and furniture with a cloth dipped into liquid disinfectant (5 per cent chloramine solution). Adequate ventilation is essential.

The best method of disinfection is by boiling. The patient's crockery and cutlery should be soaked in boiling water for 5 to 10 minutes, as should his underwear, bedclothes and washable clothing. The rest of his clothes should be regularly aired and ironed. The most common disinfectant is chloramine. When dissolved, it is a colourless and odourless transparent liquid with good disinfective qualities and, moreover, harmless to the objects on which it is used. Tubercle bacilli die within 4 hours of treatment with a 5 per cent chloramine solution.

In routine disinfection special attention should be paid to the sputum. Prior to use, a pocket-size spittoon should be third-filled with a 5 per cent chloramine solution. It should be emptied daily and boiled for fifteen minutes in a metal vessel with a 2 per cent soda solution. This can be done either by the patient himself or by adult members of the family on instructions from dispensary personnel.

Terminal disinfection is carried out when the patient leaves the premises for long periods (when he enters a hospital or sanatorium, or moves) or upon his death. The entire household, including furniture, outer clothes, bedclothes and all objects in contact with the patient, is treated. In the U.S.S.R. antiepidemic stations use special equipment to carry out terminal disinfection. Following terminal disinfection, it is useful to carry out what may be called "sanitary repair"—whitewashing the walls, changing the wallpaper, repainting the floors, windows and doors.

The patient's room should be protected against flies. In the Soviet Union all commensals, i.e., contacts, are notified at antituberculosis dispensaries and examined at least twice a year, four times a year in the case of children. A check is kept on contacts for two years after the cessation of bacillarity in the patient or his departure.

SPECIFIC PREVENTION (BCG)

Specific prevention is based on the antituberculosis vaccine discovered by Calmette and Guerin in 1921, who succeeded in isolating a strain of bovine tuberculosis called BCG (Bacillus of Calmette and Guerin), whose virulence was attenuated by multiple recultivation on a bile-containing medium (continued for 13 years), its immunogenic capacity remaining intact. The resultant liquid vaccine comprising an attenuated strain of live mycobacteria was first proposed and employed for specific prophylaxis in newborn infants in 1926. Following Calmette and Guerin's first proposals, extensive research was done on the discovery throughout the world In the U.S.S.R , antituberculosis vaccination of the newborn is compulsory. Vaccination of older age groups and negative tuberculin reactors above thirty is also extensive. Revaccination is envisaged within 2 to 4 years of primary vaccination of the newborn.

Until recently, vaccination of the newborn was effected chiefly by means of liquid vaccine administered per os. Today it is carried out just as successfully with a dry vaccine manufactured in the U.S.S.R. The immunogenic value of dry vaccine is not inferior to that of the liquid variety. Post-vaccination allergy, which is determined by the intensity of tuberculin reaction, is observed with almost equal frequency among children vaccinated by both methods.

As regards other methods of administration, viz., subcutaneous, intradermal, and percutaneous (scarification), it may be noted that subcutaneous vaccination is almost never used because of possible complications. Scarification and intradermal injection methods are universally employed for preventive vaccination.

The intradermal method has been used more extensively recently in the vaccination and revaccination of adults and children. It permits more precise dosage and ensures more pronounced and lasting immunity.

The effectiveness of antituberculosis vaccination has been proved beyond doubt Morbidity among children vaccinated against tuberculosis is from 4 to 6 times lower than among the unvaccinated Thus, along with preventive sanitary measures, the physician now possesses a powerful means of specific prevention which has played a significant part in reducing morbidity and mortality from tuberculosis

Procedure Applied in Antituberculosis Vaccination

In compliance with the order issued by the Minister of Public Health of the U S.S R. (No. 290, 1962), intradermal vaccination is to be applied universally The dosage is 0.02 mg per 0.1 ml for the newborn and infants, and 0 05 mg per 0.1 ml for children of other ages, adolescents and adults The preparation used is a dry BCG glutaminate vaccine prepared by the Gamaleya Institute of the Academy of Medical Sciences of the U.S.S R. The BCG vaccine is applied to the outer surface of the upper third of the left shoulder after preliminary alcohol treatment of the skin BCG vaccine solution (0 1 ml) is injected by means of a one-gram syringe Injections of greater amounts are not to be made Injection is accomplished *strictly intradermally* since penetration of the solution beneath the skin may lead to the formation of a cold abscess.

At peioral vaccination of the newborn, the vaccine is introduced per os in three issues on the 3rd, 5th and 7th (or 4th, 6th and 8th; 5th, 7th and 9th) days of the infant's life A 10 mg dose of dry vaccine is dissolved in 2 ml of freshly boiled or distilled water and mixed with 3 to 5 ml of maternal milk The mixture is thoroughly shaken and carefully, in small portions applied from a teaspoon, administered to the child 20 to 30 minutes prior to the next meal. During administration the head and upper part of the body must be slightly raised.

If for some reason vaccination has not been done at the mentioned date, it is carried out later by the same procedure, if the child is less than 2-months-old. Vaccination of children at any age above two months is done intradermally or percutaneously, like revaccination, with preliminary tuberculin skin tests (Montoux 1·2,000). In percutaneous administration the dose of dry vaccine (20 mg) is dissolved in 1 ml of water.

Children from tuberculous domiciles are isolated for two months following vaccination.

Contraindications to vaccination include: temperature rises above 37 5°C; persistent regurgitation; marked dyspeptic trouble; all diseases affecting general well-being (pyodermia, pemphigus, skin abscesses, phlegmona, otitis, influenza, pneumonia, etc.); obvious clinical symptoms of birth trauma. Premature birth is not a contraindication provided the child weighs more than 2 kg.

Contraindications for revaccination of non-infected children and adults are acute infectious diseases including reconvalescence, not less than two months after the disappearance of all clinical symptoms; febrile conditions, acute intestinal disturbances; hemopoietic diseases;

pernicious anemia, leukemia and hemophilia; diabetes millitus; acute nephroso-nephritis, pyuria; cardiac valvular lesions in the stage of decompensation; allergic conditions; rheumatism in the acute and subacute stages, asthma; food intoxications, and other idiosyncrasies; spasmophilia; past infectious diseases of the central nervous system (encephalitis, meningitis).

Children subjected to prophylactic vaccination for smallpox, may be revaccinated for tuberculosis not earlier than 2 months after the last vaccination, and after vaccination for polyomielitis—in a month. Children subjected to BCG vaccination may be vaccinated for other diseases only after two months have elapsed.

ORGANISATION OF TUBERCULOSIS CONTROL. ANTITUBERCULOSIS DISPENSARIES

Organised nation-wide tuberculosis control began in the U.S.S.R. only after the Great October Socialist Revolution. In pre-revolutionary Russia tuberculosis control was the concern of a public philanthropic organisation known as the Antituberculosis League. Its activity was negligible owing to restrictions imposed by the tsarist government, and it had only limited funds at its disposal. At first the Soviet antituberculosis organisation was based on the principles of West European institutions (sanitary prevention methods, etc.), developing and adapting them to the needs and conditions of a socialist state. The result was the creation in the Soviet Union of an extensive antituberculosis system including more than 5,500 dispensaries and tuberculosis departments at general hospitals and outpatient clinics, and a substantial number of specialised tuberculosis hospitals and sanatoria.

The basic unit of the antituberculosis organisation is the dispensary. In contrast to their prototype—the first dispensary established in 1887 by Robert Phillip (Scotland), or the early institutions of its kind set up by Calmette in France, Brüning in Stettin, Germany, and other West European establishments, Soviet dispensaries organise tuberculosis control throughout the districts under their supervision, conducting medical, sanitary and antiepidemic activities themselves. The antituberculosis system consists of district, city, regional and republican dispensaries, each of which caters for the entire population of its area, as well as for local industrial enterprises and other institutions. Depending on the size of the population in the particular area, there are six different categories of dispensaries. Regional, republican, urban and district dispensaries carry out methodological supervision of the antituberculosis institutions situated in their respective areas.

The antituberculosis dispensaries have the following objectives:

1. Programming of preventive measures, for which comprehensive plans are drawn up each year, laying down the population groups to be vaccinated and re-vaccinated against tuberculosis (BCG inoculation) and the schedule of mass surveys for early detection. All the medical and prophylactic institutions in the area (hospitals, outpatient

departments, medical stations at separate enterprises, maternity homes, children's institutions) participate and co-operate in this work. The plan incorporates expansion of the antituberculosis system, measures for improving working and living conditions, especially for bacillary patients, education of new personnel, organisation of refresher courses for general practitioners, sanitary propaganda, and occupational rehabilitation of post-convalescents.

2. Accomplishment of sanitary and preventive measures in centres of infection in collaboration with the antiepidemic station. Such centres are regularly visited by district nurses (at least once a month) who give instructions and supervise routine disinfection, supply disinfectants and summon contacts to the dispensary for examination. The district phthisiologist also periodically visits infection centres for prophylactic purposes.

An equally important aspect of the dispensaries' activity is therapy. They are responsible for the notification of all adult and childhood cases of tuberculosis and take all the therapeutic measures required, partly at the dispensary itself which has special departments for the purpose. In the main, however, tuberculous patients are hospitalised in specialised clinics and sanatoria at the request of dispensaries. In this way, continuity of treatment and follow-up is ensured through a succession of institutions (dispensary-hospital, sanatorium-dispensary). Therapeutic activities include recommendations on occupational conditions and behaviour and practical matters connected with the employment of patients compelled to change their occupation or working conditions.

Keeping exhaustive records of the total number of tuberculous patients and the results of treatment, the dispensary analyses per capita morbidity which is of vital importance in planning antituberculosis activities and estimating the effectiveness of the measures adopted.

Antituberculosis dispensaries are likewise responsible for the notification of all contacts. Systematic follow-up of contacts, instruction in prophylactic hygiene and periodic examination for early detection of new cases promote the reduction of epidemiological hazards.

The dispensaries pay considerable attention to children as a section of the population most frequently exposed to tuberculous infection. Tuberculin diagnosis of early age population groups is carried out annually, and for children up to 4 years of age twice a year. Day-time sanatoria are organised for weak children under the auspices of dispensaries. Children in numerous kindergartens, nurseries, children's homes, children's cultural establishments and schools are under systematic observation. As a rule, all children with local forms of tuberculosis are kept at hospitals or sanatoria until the disease is completely arrested.

The organisation of sanatorium-type nurseries, kindergartens and forest schools for tuberculous children, as well as boarding-schools for

children with tuberculous environments is of major importance for the prevention of childhood tuberculosis.

The dispensary structure varies according to the scope of its activity and may include departments for adults and children, specialists in various forms of tuberculosis (bone-and-joint, laryngeal, etc.). There are many diagnostic services, such as X-ray installations and laboratories equipped for microbiological research. The dispensary services a particular district, one district phthisiologist supervising 30,000 to 35,000 inhabitants and all local enterprises and institutions. For every two phthisiological districts there is one pediatrical. The phthisiopediatrist supervises all children's institutions in his area. The antituberculosis dispensary maintains close contact with all the medical and prophylactic institutions in its area.

CHAPTER XII

HYGIENIC AND DIETARY TREATMENT

Modern antituberculosis therapy is very efficient, particularly when dealing with pulmonary cases Recovery is common today, provided the right method is adopted and treatment commences in time. The physician has a wide range of potent antibiotics and chemotherapeutic drugs at his disposal, as well as various methods of collapse therapy and surgical treatment. Nevertheless, the basic premise of success is an individually chosen and strictly observed hygienic and dietary regime ensuring elimination of metabolic disorders and increasing the general powers of resistance

Strict rest in a hospital or sanatorium during the acute period of the disease under adequate chemotherapy paves the way to successful results in treatment. During quiescence, convalescence and readjustment to occupational requirements, rest will promote the stability of therapeutic results

Hygienic and dietary therapy envisages the following individually prescribed general supportive measures

1. Aeration therapy indoors, on verandahs or out-of-doors, depending on the patient's condition and the season;

2 Adequate diet, appropriate to the stage of the disease and taking into account the individual clinical features in every given case (age, form and stage of disease) and, in particular, the existence of ailments, such as diabetes, thyreotoxicosis, dyspeptic symptoms, etc.,

3. Physical therapy, including climate therapy; most important in this respect are systematic and strictly graduated measures promoting resistance to temperature changes: hydrotherapy in the form of cold sponging in the morning and, with stable compensation, shower-baths of suitable temperature with subsequent bed-rest, etc.

In addition, it must be stressed that the tuberculous patient should meticulously observe the rules of personal hygiene to build up his general resistance

AERATION THERAPY

Aeration therapy is extremely important in treating all forms and localisations. It should always be remembered that the active stage of tuberculosis involves various disturbances on the part of the central

nervous and endocrino-vegetative systems (neurasthenic syndrome) associated, primarily, with tuberculous intoxication arising from assimilation of the products of tubercle bacilli metabolism and tissue decay. The toxic substances assimilated from inflammatory foci affect the central and vegetative nervous systems, leading to changes in reaction and presenting one of the primary causes of metabolic disturbances. If we consider, in addition, that pulmonary tuberculosis is accompanied by a varying degree of changes in the cardiovascular function as well as hypotension and tachycardia with hypoxemic symptoms, it becomes clear why such stress is laid on the utilisation of fresh air as a powerful curative and tonic factor. Air therapy helps to normalise external respiration, being an excellent general and nutritive stimulant with a favourable influence on appetite and sleep. It will be relevant here to recall the words of I. P. Pavlov, who, when formulating the concept of food in his lectures, named the oxygen inhaled at respiration as one of its components.

As stated earlier, tuberculous infection and intoxication result in disturbances of gas exchange (external and internal respiration). In both, acute and chronic, cases we have to deal with a varying degree of oxygen deficiency, which confirms the importance of air therapy in the general antituberculosis arsenal. As V. A. Vorobyov, one of the founders of Soviet phthisiology, correctly pointed out, out-of-door sessions are a powerful general tonic strengthening the body's resistance to temperature changes.

The treatment of tuberculosis in the active stage requires suitable conditions. In some cases, attacks and exacerbations necessitate hospitalisation, while in others they call for sanatorium treatment, which in the U.S.S.R. is available at state expense for the full period required in each case. Sanatoria offer the most favourable conditions for establishing an adequate regime utilising all the potentialities of aeration therapy. In the active period, the patient should be offered an opportunity of mental and physical rest—from strict bed-rest in the acute stage to indoor maintenance in quiescence. Regular ventilation of the premises (open casements or windows in the warm season) is extremely important. Subsequently, the patient should spend regular periods out-of-doors, resting on properly equipped and protected verandahs, with moderate movement and walks during recovery. Graduated out-of-door exercise, such as easy gardening, is also useful.

When more or less stable compensation is attained, therapeutic physical training is advisable, with respiratory exercise under the control of a physician in indicated cases. It should be remembered that any movement prescribed for therapeutic purposes has a certain effect on metabolism, but when excessive, it is liable to activate the tuberculous foci.

Out-of-door maintenance throughout the 24 hours is ideal, but in the moderate belt, it is unfortunately practicable only in summer.

Aeration therapy is usually administered in parks and woods, or else on special verandahs on sanatorium premises, sometimes offering

direct access to the verandahs from the patients' wards. As mentioned earlier, verandah maintenance is alternated with graduated bed-rest which is prescribed individually according to the form and stage of the disease. The patient must return to bed strictly at the appointed time.

Verandah rest is usually prescribed at compensation or incipient quiescence. In the acute stage, strict indoor bed-rest is recommended, taking into account the conditions required for the treatment of the disease.

MODIFICATIONS OF SUPPORTIVE REGIME

The combination of therapeutic measures is chosen individually, in accordance with the different periods (stages), viz., acute attacks, exacerbation, quiescence. In all, there are three types of supportive regime:

1. In the acute stage, during attacks or exacerbation, i.e., in the period of clear decompensation—strict bed-rest and complete mental and physical relaxation;
2. During quiescence and developing subcompensation relative rest with aeration therapy: relaxation on a verandah, short walks;
3. During stable compensation—graduated exercise, therapeutic physical training, aeration therapy.

Generally speaking, the process of treatment presents a controlled transition from rest via exercise to occupational activity. Regular graduated exercise is prescribed not only during institutional treatment, but in the period of adjustment, i.e., return to occupational activity.

Supportive Regime in Acute Stages and Exacerbation

Strict bed-rest is prescribed in acute pneumonic attacks, acute and subacute hematogenous dissemination, especially with the meningeal localisation, at exacerbation of old fibrous and fibrocavernous lesions, on tuberculous pleurisy with effusion, and pneumopleuritis. In other words, such a regime is indicated in all cases characterised by a febrile condition and intoxication manifestations (fever, nocturnal sweating, weakness, etc.). Besides that, strict bed-rest is necessary as an emergency measure in hemoptysis, spontaneous pneumothorax, pain syndromes (dry pleurisy) and other complications.

Complete mental and physical relaxation is aided by the entire atmosphere of the medical institution adapted to the particular requirements of tuberculous patients. The patient is kept at an even warm temperature, a permanent supply of fresh air being ensured. The diet is drawn up to suit the individual features of each given case.

Personal hygiene, skin hygiene and bed hygiene should be observed meticulously in all cases. While temperature returns to normal, it is

necessary to resort to the tonic effects of sponging the entire body with water at room temperature beginning with the hands, then passing to the chest, abdomen, legs and back which is usually, such sponging being done in bed in the morning, to be followed by bed-rest for at least 20 minutes

In the acute period a sparing diet is prescribed, ensuring, however, full compensation of expended energy. Special attention should be paid to the regularity of intestinal functions. Constipation is precluded by an adequate mixed diet including vegetables. The diet is one of the most important supportive factors. Overeating should be avoided by all means. Four or five meals a day will best suit the purpose.

Quiescence and Subcompensation

In a number of cases, subcompensation is marked by continuing nervous hypersensitivity, fatigue and hypotension In such cases a careful transition from bed-rest to room and verandah maintenance is recommended. This provides conditions for heightening the patient's general tone, improving his metabolism and vegetative functions—sleep, appetite, etc. At normal temperature, the patient is allowed short out-of-door walks under constant temperature and pulse control.

Exercise at Compensation

During recovery, when the lesions are stabilised and moderate physical exertion and work do not cause temperature rises or sharp fatigue, careful exercise is allowed In sanatorium conditions, this implies an alternation of rest and exercise, with elements of therapeutic physical training. The patient is permitted to take walks, beginning with 15-20 minutes and gradually extending in length to one or two hours a day. In indicated cases, easy forms of work like gardening are prescribed. However, if a rise in temperature is noted after a walk, exercise should be prescribed with caution

In this period, exercise should alternate with hours of rest Lying on an open verandah for up to four or five hours daily is an extremely important factor in obtaining stable recovery.

Adjustment to Occupational Activity

During clinical recovery, the patient has to be re-adjusted to occupational activity, which involves a choice of occupation conforming to his condition. Through this period he is kept under permanent dispensary follow-up and is to be provided with adequate occupational conditions, sometimes even involving a change of profession. When time has proved his recovery stable, the patient returns to his usual job, remaining, however, in the third group of dispensary notification.

DIET

The diet for tuberculous patients should include various nutritive substances of adequate quality and quantity to meet the increased expenditure of energy occasioned by the infection and the tuberculous process. The basic diet should provide a varied combination of both animal and vegetable products, as well as minerals and vitamins.

It is essential that the diet consist of the necessary amount of proteins, fats and carbohydrates in correct proportions and a sufficient range of auxiliary substances such as vitamins A proper supply of vitamins in the food ensures the most effective assimilation of proteins, fats and carbohydrates On the average, 2 g of proteins, 1.5 to 2 g of fats and 7 g of carbohydrates are required daily per kg of body weight.

Biologically, adequate proteins (containing such amino acids not synthesised by the organism as phenylalanine, tryptophan, methionine, etc), should comprise 15 to 20 per cent of the total calory intake. The amount of calories required by the tuberculous patient usually varies from 3,000 to 4,000, depending on age, sex, form and stage of disease, as well as weight deficiency

In the acute period and during exacerbation, as mentioned earlier, there is an increase in energy expenditure and protein disintegration, which is associated with the febrile syndrome However, in persistent febrile conditions and with a drastic reduction of body weight, there is a tendency towards economy of protein, the protein metabolism in these cases depending to a greater extent on malnutrition than on the febrile condition The degree of digestion of the overall food intake is just as important as the intake proper Here we must again stress the significance of a diet rich in vitamins as best helping the assimilation of proteins The patient should eat a daily average of 120 to 130 g of proteins, of which no less than half should be of animal origin.

It is inadvisable for the patient to have too much fat, the required amount varying from 70 to 100 g daily, depending on his condition. This quantity of fats helps to eliminate weight deficiency In addition, fats contain the lipovitamins A and D. The best kind of fat is, of course, butter. Vegetable fats, in particular sunflower oil as a source of unsaturated fatty acids (linolic and linolinic), are also essential.

The recommended quantity of carbohydrates is from 400 to 500 g. They are a vital nutritive factor, especially during adjustment to occupational activity. Glucose is a widely-known carbohydrate essential for the nervous system, which it supplies with oxygen. An excess of carbohydrates, however, is also inadvisable. Only in certain cases (anorexia) should a higher concentration of carbohydrates, mainly in the form of jam, honey, etc., at breakfast, be prescribed for two or three weeks.

Vegetables and fruit not only provide an adequate supply of vitamins, but are a source of essential mineral salts containing sodium,

potassium, phosphorus, etc. Disorders of mineral metabolism in tuberculosis are usually accompanied by wasting. Thus, the maintenance of a proper mineral balance necessary for normal body function depends on an adequate diet containing a sufficient amount of vegetables and fruit. The most important of the vitamins are vitamin C (ascorbic acid), A and the B group. A dietary deficiency of vitamin sources should be compensated by the addition of the respective vitamins in pure form, in the first place vitamins A and C and various representatives of the B group. The prescription of polyvitamins is also essential, since the preponderance of any individual substance may upset the overall vitamin balance.

In the case of vitamin C, its content is known to be reduced during the active period. The level of vitamin C in the blood varies from 0.55 to 0 80 mg% Concentrations below 0.40 mg% are pathological, calling for an addition of vitamin C to the diet. Vitamin C improves the nutrition of the blood vessels, having a regulative effect on their permeability, as well as on hematopoiesis, iron and calcium metabolism, etc. Apparently, it also plays a part in the production of steroid hormones. Vitamin C is stored in the liver and, chiefly, in the adrenals and pituitary. Replenishment of the supply of vitamin C is of vital importance. The best means of overcoming vitamin C deficiency in tuberculosis is a rich vegetable diet. (The content of vitamin C in various products is given in the table drawn up by the vitamin laboratory, All-Union Institute of Plant Growing, Fig. 64).

Occasionally, however, it is necessary to add pure vitamin C in the form of ascorbic acid, especially when there is a tendency to different dyspeptic disorders. In healthy adults, the daily vitamin C requirement is 50 to 75 mg. In tuberculosis the respective figures are from 200 to 500 mg.

The tuberculous process, like any other infectious disease, leads to a deficiency of vitamin A, the lack of which causes general lassitude with increased permeability of the mucosa and a reduction of the latters' general resistance to infection. The daily intake of vitamin A for healthy individuals comprises from 2,000 to 4,000 u. To eliminate A-vitamin deficiency 6,000 to 7,000 u and more are required.

Part of the required vitamin A is obtained in ready form from products of animal origin, but most of it is produced in the body from provitamin A—carotene. Carotene is found in carrots and other vegetables as well as in some fruits. However, the importance of carotene is not limited to its being the source of vitamin A. There are indications that carotene itself plays an important role, stimulating metabolism.

Besides vitamins C and A, another important substance is the antirachitic vitamin D whose physiological function is associated primarily with calcium and phosphorous metabolism, which is essential in tuberculosis One to two tablespoonfuls of cod liver oil daily added to the food as a source of vitamin A, will likewise help to cover the requirement in vitamin D.

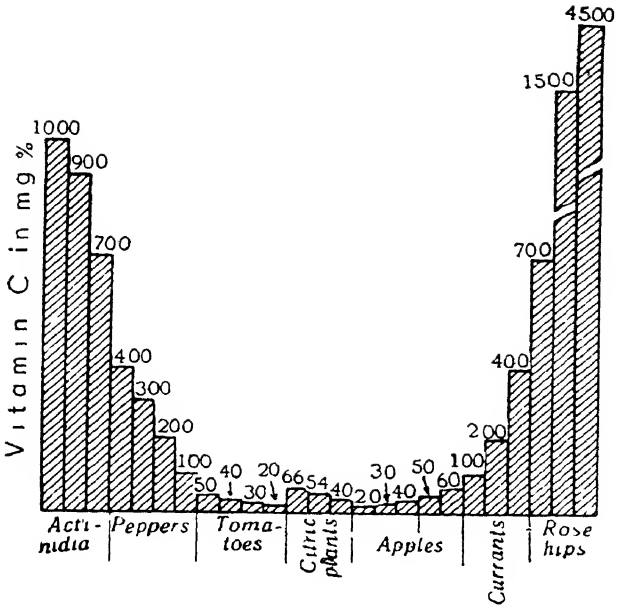


Fig. 64. Content of vitamin C in various strains of fruit, berries and vegetables Figures show content of vitamin C in mg of ascorbic acid per 100 g of products (from Vitamin Laboratory, All-Union Institute of Plant Growing)

Vitamins of the B group, in particular, B_1–thiamine, and B_2–riboflavin, are also essential. Vitamin B_1, which helps to regulate the carbohydrate and protein metabolism, also stimulates the assimilation of sugar and calcium, accelerating oxidative phosphorylation and purine metabolism. Owing to the excessive expenditure of thiamine in tuberculosis, it should be administered in daily doses of 10 to 30 mg internally.

Riboflavin takes part in the redox reaction, i.e., cellular respiration, as well as protein and lipid synthesis. In tuberculosis, the riboflavin metabolism is impaired, which necessitates administration of riboflavin in doses larger than normal–from 5 to 10 mg and more daily–especially in functional disorders involving the gastrointestinal tract.

An adequate mixed diet including proteins, fats, carbohydrates and the entire range of vitamins and mineral compounds in a quantity sufficient for the requirements of the given organism and allowing for weight deficiency, is essential in the treatment of tuberculosis. It should be emphasised that the degree of digestion of the overall food intake is no less important than the intake itself. The vegetative functions, in the first place appetite, are best stimulated by air therapy. With adequate respiration, the patient eats well and digests his food properly.

CLIMATE THERAPY. KUMISS

Climate therapy is often of considerable use in the treatment of tuberculosis. Such alpine sanatoria as Teberda (1280 to 1420 m above sea level) and Abastumani (1270 to 1350 m) in the U.S S R or Davos in Switzerland, enjoy justified renown as valuable climatic resorts. The dry mountainous climate with dust-free rarefied air, low precipitation, cool summer and moderately cold winter temperatures, as well as high solar radiation, may be utilised as a potent tonic increasing resistance to low temperature Their effects are especially beneficial in perpetuating the therapeutic results obtained in the native climate. Patients badly affected by the interim seasons at home and not evincing good results after local treatment, are usually sent to southern seaside resorts. On special prescription, some patients from the central and northern regions of the U.S S.R., where spring and autumn weather contrasts heavily tax their adaptive resources, are treated in the sparing environmental conditions of the southern coast of the Crimea. Stronger patients with quiescent processes are sent to alpine climate sanatoria (1200 to 1400 m above sea level) in summer and winter, to avail themselves of the local general supportive and tonic factors (dust-free rarefied air)

Climate therapy can occasionally be used as a general supportive means, when measures taken locally fail to produce benificial results or when such results have to be substantiated Some patients respond favourably to kumiss, a valuable dietetic product obtained by fermentation of mare's milk. The fermentative agents are *Bacillus orenburgii* and *Torula kumys.* The first of these partly ferments the lactic sugar, forming lactic acid, and splits proteins into polypeptides *Torula kumys* inverts the sugar, fermenting it with the producton of alcohol and carbon dioxide. Kumiss may be strong, medium or mild, depending on its alcohol and lactic acid content. The drinking of kumiss, especially in steppeland climate, enhances general nutrition.

But, of course, the most essential factor in prolonged therapy of tuberculosis is rational sanatorium treatment with observance of a strict supportive and protective regime. Hence, the principles of local treatment, preferably under customary climatic conditions, justifiably advocated by V. A. Vorobyov and T. P. Krasnobayev, remains valid to this day.

Without doubt, success in all methods of treatment, including chemo therapy, surgery, etc., is promoted by a correctly prescribed and maintained sanatorium regime.

CHAPTER XIII

ANTIBACTERIAL THERAPY

The rise of modern antibacterial therapy is associated with the discovery of antibiotics—organic substances produced by microorganisms in the struggle for existence, antagonising and suppressing the growth and development of microbes. At present, however, antibacterial therapy incorporates the use of both antibiotics and synthetic chemical drugs. This is all the more justified since the boundaries between the two types of drugs are progressively disappearing. The structural formulas of natural antibiotics have become known and their synthetic analogues are being manufactured

The discovery of penicillin by Fleming in 1928 led to remarkable achievements in the treatment of a number of suppurative diseases and pneumonia, also promoting research in other directions. When S. Waksmann, Schatz and Bugie (1944) succeeded in isolating from *Streptomyces griseus* a substance with the typical properties of an antibiotic which they named streptomycin (Fig. 65), physicians received a new drug which exerted a bacteriostatic effect on the tubercle

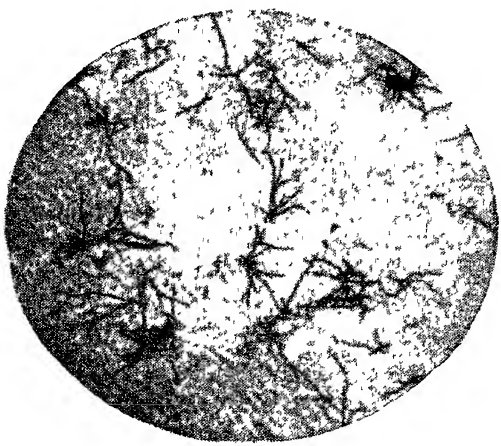


Fig 65 Streptomyces griseus—strain producing streptomycin

bacillus. Streptomycin has now been used for almost 20 years in the clinical treatment of various forms of tuberculosis and, especially, its most frequent pulmonary localisation.

Yet, apart from streptomycin with its comparatively rapid effects, the later developed synthetic drugs belonging to the group of hydrazides of isonicotinic acid, acquired still greater importance not only due to their convenience, but by virtue of their physico-chemical properties demonstrated in their effects on microbes *in vivo*.

Streptomycin and the hydrazides of isonicotinic acid (phthivazid) became the basic antituberculosis drugs to be applied individually. However, the separate application of these drugs is limited, firstly, by the development of microbial drug-resistance, and secondly, by the toxico-allergic side effects which they provoke in certain cases. To permit the long-term treatment, commonly required, use is made of different drug combinations, mainly including sodium paraaminosalicylate (P.A.S.) proposed by Lehman. Combined chemotherapy delays the development of microbial drug-resistance. The question of the side effects produced by these drugs will be dealt with further.

In antibacterial therapy account should be taken not only of the bacteriostatic effects of the drugs, but their influence on body reaction.

It is quite obvious that after the reproduction and vital activity of the microbes are suppressed the disease is overcome by the same bodily protective powers which cause the development of immunity to the given disease and the subsequent healing processes

As a rule, chemotherapy is most successful when it is commenced in institutional conditions under an adequate general supportive regime.

Extramural therapy cannot serve as a substitute for sanatorium treatment, being only a continuation of therapy to be applied along identical lines during quiescence.

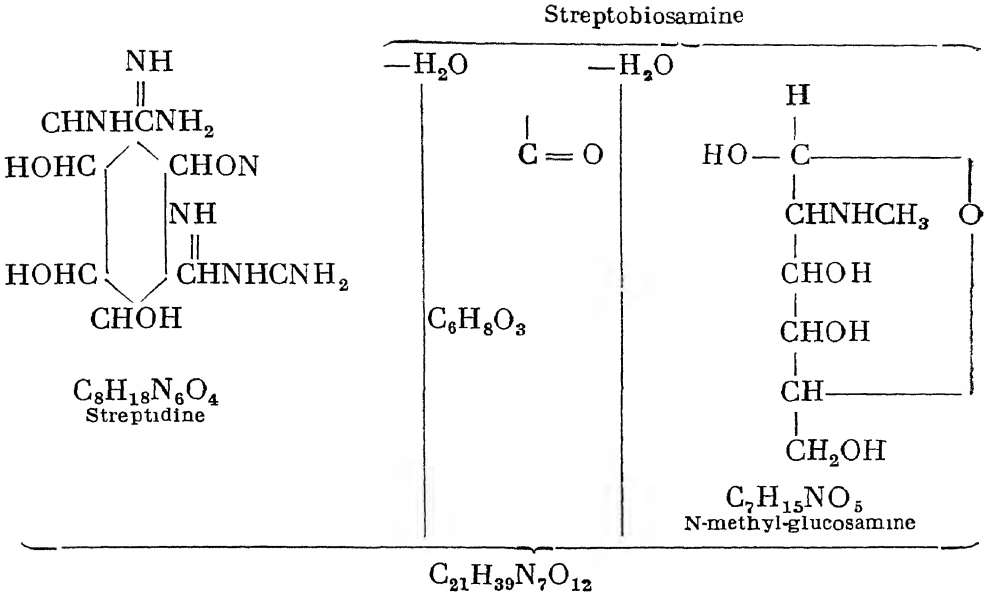
PRIMARY DRUGS

Streptomycin

Streptomycin ($C_{21}H_{39}N_7O_{12}$) is an organic hydroxylised base—streptidine—with a considerable nitrogen content. Streptidine is glucosidally linked to a nitrogen-containing disaccharide-like group, which contains carbonyl—glucosamine groupings.

The structural formula of streptomycin, as given by Waksmann, is presented below.

Glucose is contained in streptomycin in the form of an optical polymer not known to exist in nature. A sterile dilution of the drug retains its activity at 37°C for 15 to 17 days. It is readily soluble in water, also dissolving in ether, chlorophorm and acetone and has no affinity to lipids. An essential point is that its activity is dependent on the composition of the medium in which it acts. The optimum pH for



streptomycin is from 8 to 8.2. According to Freerksen, the concentration of streptomycin in different organs in the first four hours after administration of 1 g of the drug, is as follows (γ per ml):

kidneys	28
blood	22
larynx	10
lungs	8
walls of the large intestine	6 5
lymph nodes	4.0
bones	2.5

Approximately 50 to 75 per cent of the streptomycin administered is discharged through the kidneys (glomerular secretion) in 24 hours. The optimum blood concentration, after R. O. Drabkina and Y. P. Sinelnikova, resulting from a single administration of 0.9 to 1.2 g of streptomycin, is 40 u per ml.

1 ml of crystalline streptomycin contains 1000 units (1 γ of the pure base containing one unit).

In medical practice, streptomycin is applied as a chlorhydrate (*Streptomycinum hydrochloricum*), sulphate (*Streptomycinum sulfuricum*) or crystalline chlorocalcium compound (*Streptomycinum cristallisatum*) used for intralumbar injection. In the Soviet Union extensive use is made of streptomycin sulphate. Another compound employed is dihydrostreptomycin obtained by reducing the free aldehyde group to an alcohol group on the streptose side of the molecule. Streptomycin is low-toxic and, if histamine-free, comparatively seldom has side effects.

Dihydrostreptomycin should be used with caution, after thorough examination of the auditory apparatus, whose function may be seriously affected by the drug.

In vitro, streptomycin shows a marked bacteriostatic effect. In doses of 0 5 to 1.0 (10 to 20 mg per kg of body weight) when injected intramuscularly, especially at optimum blood concentrations (approximately 40 units per ml), streptomycin has a marked bacteriostatic effect on the tubercle bacillus. In general, it is a wide-spectrum drug, having a bacteriostatic influence on streptococci, staphylococci and other microbes.

Rp Streptomycini sulfurici 1 0 (1 000 000 u)
D t d. N X
S For intramuscular injection

Along with intramuscular injection, in certain cases, for example, in tuberculous meningitis, streptomycin is administered intralumbarly, in lesions of the respiratory tract—intratracheally or as an aerosol. In addition, it may also be introduced intrapleurally. Intralumbar injections are usually made with 100,000 to 200,000 units accompanied by an intramuscular injection of 1 000 000 units.

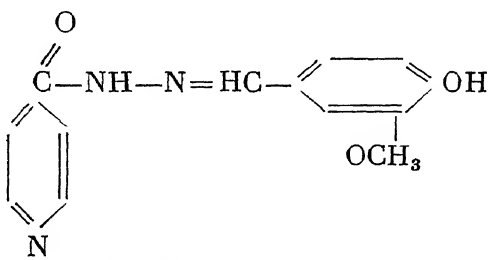
Streptomycin aerosol produces good results in tuberculosis. The drug's effectiveness in such treatment depends on the physical characteristics of the aerosol. Granulometrically, the myceles are 0 5 to 3 microns in size. The particles are electrically negative, their surface tension being lower than that of water. According to Paraf and Zivy, 2.5 ml of streptomycin solution containing 50 000 u per ml is employed per inhalation. The drug is rapidly assimilated, the assimilation rate being comparable with that of intraarterial administration With an absence of side effects, inhalation is conducted for 1 to 3 months together with intramuscular administration According to instructions by the U.S.S.R. Ministry of Public Health, children are prescribed streptomycin in doses of 0 015 to 0 02 g per kg of body weight, and adults 0 5 to 1 g daily

Antibacterial therapy for tuberculosis is based on the principle of microbe antagonism, well known since the days of I. I. Mechnikov, who stressed the importance of this phenomenon Streptomycin, when used clinically in different forms of tuberculosis, pulmonary and otherwise, has proved highly effective, from the very start producing good results in such severe diseases as acute miliary tuberculosis and tuberculous meningitis. Subsequent experience demonstrated its efficacy in chronic forms as well. However, experience showed that with time, when used separately, streptomycin tends to lose most of its effects After 3 or 4 months' treatment the microbes become immune to the drug Mycobacteria growing at drug concentrations exceeding 10 γ per ml of medium are considered resistant. Those showing signs of growth at concentrations of 100 γ per ml are said to have absolute resistance, while strains growing at concentrations of 10, 25 and 50 γ per ml are known as relatively resistant. In some cases, strep-

tomycin-resistant microbes become so accustomed to the effects of the drug that so-called streptomycin-dependence and streptomycinophilia develop, under which the growth and development of tubercle bacilli are even intensified by the application of streptomycin.

The Group of Hydrazides of Isonicotinic Acid (INH): Tubazid (Isoniazid), Phthivazid, Saluzid and Others

Drugs from the group of hydrazides of isonicotinic acid, on the basis of enormous clinical and dispensary experience are justly regarded as the cornerstone of modern antituberculosis chemotherapy. The Soviet drug phthivazid (isonicotinoyl hydrazone-vaniline (see structural formula) was developed by M. N. Shchukina, Y. D. Sazonova, G. N. Pershin, O. O. Makeyeva in 1951-52. The drug offers a good example of the hydrazide group and is extensively used today. In a concentration of 1:16 000 000 in Soton's medium, phthivazid inhibits the growth of tubercle bacilli.



Phthivazid

The drug is prescribed as follows:

Rp. Phthivazidi 0 5
D.t d in tabul, N.XX
S 1 tablet two to three times a day

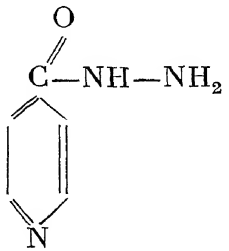
Studies of the concentration of phthivazid in the blood indicate that a single dose of 0.5 g should be regarded as optimum. When introduced orally, it concentrates considerably in the spinal fluid. Along with streptomycin, phthivazid represents one of the major antituberculosis drugs. Phthivazid therapy results in destruction of microbe protoplasm, observable by electronic microscopy, as well as chemical changes, particularly reduction of the lipid content. The mycobacteria lose their acid-fastness as well as their ability to sensitise the host organism (A. Y. Rabukhin).

Another representative of the isonicotinic acid hydrazides is saluzid.

Rp. Saluzidi 0.5
D t d. N XX
S. 1 tablet twice daily

Endolumbar injections in meningitis are made with soluble saluzid (*Sol. saluzidi*).

Another therapeutically valuable drug is isoniazid, synthetised by Fox. The drug presents a hydrazide of isonicotinic acid with the following structure



Isoniazid

A similar drug used in the U.S.S.R. is tubazid, administered in doses of 8 mg per kg of body weight, 2 or 3 times a day (from 0.45 to 0.6 pro die).

Use of the drug is followed by a swifter increase of its concentration in the blood, but also by a more rapid reduction than is true of phthivazid.

Successful clinical use is made of metazid (1.1-methylene-bis-isonicotinoyl hydrazone) and larusan (furfural acetone isonicotinoyl hydrazone).

It should be noted that the isonicotinic acid hydrazides penetrate the tissues (in particular, pathologically affected tissue barriers) much easier than do molecules of streptomycin. Their higher penetrability evidently deserves special attention.

As in streptomycin therapy, the separate use of phthivazid results in the development of resistance to the drug, probably accompanied by a reduction of the microbe's virulence. Resistance to isonicotinic acid hydrazides is stated when the mycobacteria grow at drug concentrations exceeding 1 γ per 1 ml of medium (for tubazid). Yet even in the given case, despite evidence of lowered virulence resulting from the use of isonicotinic acid hydrazides, phthivazid-resistance must be considered undesirable, limiting the therapeutic effects of the drug (M. A. Klebanov and R. O. Drabkina).

The use of the isonicotinic acid hydrazides (phthivazid, metazid, tubazid, etc.) provided new conditions and possibilities for the treatment of pulmonary tuberculosis and other localisations. They have a marked effect in exudative and infiltrative forms of tuberculosis where they promote rapid resorption of pathologic changes and disintoxication of the body as a whole. A negative pharmacological feature of these drugs is their effect on the central and vegetative nervous systems and the associated increase of cortical inhibition. They stimulate the reticuloendothelial system and show definite anti-inflammatory qualities.

Special note should be made of the disturbances of ascorbic acid and vitamin B_6 metabolism caused by the use of phthivazid, owing to which systematic additional administration of vitamin C in doses of 0.5 and more daily, as well as vitamin B_6 (pyridoxine) should be prescribed, especially if side effects appear.

New information has recently become available on the metabolic features of isonicotinic acid hydrazides, connected with the acetylisation and deep decomposition of the drug. In particular, there appears to exist a considerable category of people whose organism rather swiftly nullifies these drugs. This apparently applies to more than a third of all cases. However, the same instances show phthivazid to have certain advantages, being less rapidly discharged from the body.

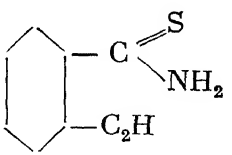
Drugs of the INH group, like streptomycin, are not used separately, but in combination with P.A.S., which precludes drug-resistance. Apart from these two basic combinations, phthivazid and streptomycin are often used together, as well as all three drugs combined.

SECONDARY DRUGS

Cycloserine, Trecator and Other Drugs

Of late, a number of new preparations including cycloserine, canamycin, ethionamid, trecator (drug 1314), ethoxide, have been proposed for the treatment of tuberculosis. Cycloserine is an antibacterial drug extracted from a culture of *Streptomyces orchidaceus* and *Streptomyces goryphalus.* The drug is used initially to assay tolerance in a daily dosage of 250 mg, and later 0.75 to 1 g during the day. In cases when primary drugs prove ineffectual, e.g., intractable cavities, this drug may be used with success.

Ethyl-thiazo-nicotin thiamide-α, ethionamid, trecator 1314 is isonicotinic acid derivative with the following structural formula:



In experiments on mice, ethionamid proves 10 times less active than isoniazid, but 8 times more active than streptomycin. There are no clinically manifest effects on the liver and kidneys. Side effects include nausea, sometimes with vomiting, and anorexia. An initial weight loss is noted occasionally during the first three or four months of treatment. Maximum concentration in the blood is observed six hours after administration of the drug and three hours after administration of the suppositorium. In all cases it should be applied in combinations, since at independent introduction bacterial resistance develops within a month. There are interesting indications of the especially benign effect of the drug in tuberculosis of the lymph nodes in childhood. The drugs

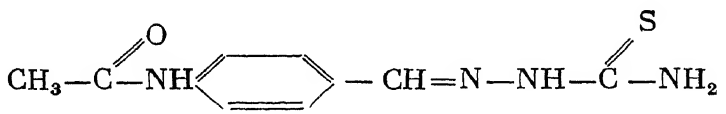
is manufactured in pills. Dosage: one pill contains 250 mg of ethionamid. It is prescribed for adults per os, 0.75 to 1 g pro die, for children, 20 to 40 mg per kg of body weight. The initial dose is usually 0.25 g pro die, increased after 5 days to 0.25 g in two issues daily, then for 5 days—0.25 g 3 times a day. The optimum dosage is 0.25 four times a day. In some cases with gastric disturbances, suppositories are prescribed: one every evening and morning.

The secondary drugs include ethoxide—4.4 diethoxidiocarbonylid. Ethoxide is prescribed internally before meals. The therapeutic dose is 1 g daily in two issues.

Canamycin is an antibiotic obtained from *Actinomyces kanamyceticus* (Umezava), extracted from the cultivation liquid of an actinomycete. It belongs to the group of antibiotics related to streptomycin, and is prescribed as streptomycin: 1,000,000 u daily in two issues. It should be noted that the use of canamycin should be preceded by audiometry owing to possible side effects on *n. stato-acustici.*

Canamycin is administered in the usual combinations with other drugs.

Apart from those mentioned as secondary drugs, tibone synthesised by Domagk is occasionally prescribed in doses of 0.05 twice daily. Due to its toxicity, the drugs use is limited.

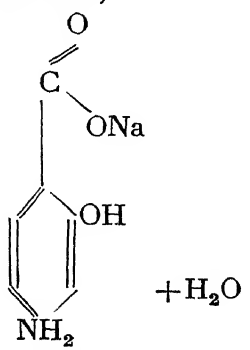


Tibone (paraacetaminobenzaldehyde thiosemicarbazone).

Secondary drugs affect *Mycobacterium tuberculosis* less than do INH and streptomycin. It is important to note, however, that they affect mycobacteria resistant to the primary drugs.

SODIUM PARAAMINOSALICYLATE (P.A.S.)

Lehman proposed the therapeutic use of sodium paraaminosalicylate (sodium 4-amino-2-oxy-benzoate).



The bacteriostatic effects of P.A.S. are evident with considerable dosage (more than 15 g daily), in a ratio of 200 mg per kg of body

weight. But even in lower quantities (10 to 12 g daily) P A.S., used together with intramuscularly injected streptomycin, considerably delays the advent of streptomycin-resistance. P.A.S. is assimilated through the intestine. Six hours following administration, 70 per cent of the drug is discharged with the urine.

The first experiment in combined antituberculosis chemotherapy using both streptomycin (0.5 to 1 g daily for adults) and P.A.S. (12 g daily) proved successful, the pathogen of tuberculosis remaining sensitive to the drug for many months.

Prescription is as follows:

Rp. Natrii paraaminosalicylici 3 0
D t.d. N XX
S. 1 powder 3 to 4 times daily, half an hour after meals, in a quarter of a glass of soda water or mineral salts (borzhom).

The results of the treatment are shown in Fig. 66. As evident, there is a rapid monthly development of streptomycin-resistance when

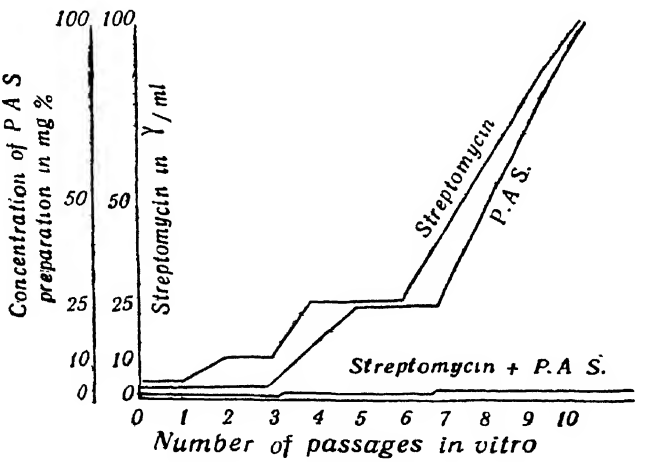


Fig 66. Increase of streptomycin- and P.A S -resistance in *Mycobacterium tuberculosis in vitro* at separate and combined administration

streptomycin and P.A.S. are used separately, whereas in combined chemotherapy resistance is considerably delayed.

On a number of occasions (fresh processes, caseous changes, etc.), doctors resort to intravenous drop injections of P.A.S. solution. The dosage amounts to 250 ml of a stable 3 per cent solution of paraaminosalicylate.

In cases of P.A.S. intolerance, BEAMS (benzacyl), a calcium salt of 4-benzo-amido-salicylic acid, is employed. It is used in a dosage of 10-14 g, taken 3 to 4 times daily with water. BEAMS is less irritating for the gastrointestinal tract and kidneys.

INDICATIONS AND CONTRAINDICATIONS FOR COMBINED CHEMOTHERAPY

The use of streptomycin is advisable in acute forms of tuberculosis. In acute miliary tuberculosis, tuberculous meningitis as well as acute pneumonic forms a triple combination is used, e.g.: streptomycin + phthivazid + P.A.S. or double combinations, such as streptomycin + phthivazid, streptomycin + P.A.S.

Treatment of the mentioned forms, if promptly begun, brings recovery in up to 90 per cent of cases. The choice of drug combination depends on the acuteness and severity of the patient's condition and the basic type of lesion. Some authorities call streptomycin a critical drug. Indeed, it is highly efficient in acute miliary tuberculosis and tuberculous meningitis when combined with drugs of the group of isonicotinic acid hydrazides. In tuberculous infiltrations, infiltrative forms with disintegration and fresh cavernous lesions, both streptomycin and phthivazid, taken separately or in combination with each other or P.A.S., are highly active drugs promoting the closure and collapse of cavities. Continuous chemotherapy closes fresh cavities in 80 per cent of all cases. Fibrocavernous tuberculosis, especially of long standing, or incapsulated caseous foci (e.g., tuberculomata) are not readily amenable to streptomycin. This form is most successfully treated by phthivazid, tubazid or methazid in combination with P.A.S., especially when there is need to arrest and remove the exacerbations occasionally arising in fibrocavernous tuberculosis of the lungs.

Combined chemotherapy, primarily with the use of streptomycin, is successfully employed in various extrapulmonary localisations of tuberculosis, viz., intestinal lesions, when streptomycin combined with phthivazid leads to the healing of ulcers and normalisation of intestinal secretion and motility. Streptomycin, in combination with P.A S., has an extremely beneficial effect in lesions of the upper respiratory tract, larynx, trachea and bronchi, and no less so in primary lesions of the urogenital system.

The effect of streptomycin and even phthivazid with P.A.S. is less marked in caseous lesions of the lymph nodes.

Combined chemotherapy employing streptomycin or phthivazid with P.A.S. is extremely effective in tuberculous lesions of the bones and joints. The continuous application of these drugs has considerably reduced the period of treatment. Augmented by general supportive treatment in specialised sanatoria, it has led to more complete recovery without causing crippling deformities of the legs.

The use of streptomycin proved highly beneficial in fistulous forms of bone-and-joint tuberculosis.

Combined chemotherapy (streptomycin + P A.S.) is especially important in surgery. The latest developments in intra- and extrathoracic surgery for tuberculosis are directly associated with the advent of antibacterial therapy. Chemotherapy is administered for at least two months prior to operation. Operations are performed under cover of

chemotherapy, continuous postoperative administration of antibacterial drugs (streptomycin + phthivazid) being absolutely necessary under appropriate hygienic and dietary measures applied in sanatoria.

It should be noted that chemotherapeutic drugs are well tolerated by pregnant women with active forms of tuberculosis. Chemotherapy is strictly indicated for them before and after childbirth.

Owing to the recent discovery of tuberculous forms resistant to the basic drugs, it is advisable to apply combinations with new drugs, particularly ethionamide (trecator 1314-th), cycloserine, ethoxide, etc., especially in cases when the mycobacteria prove resistant to the primary drugs. Most preferably, the new drugs are combined with drugs of the isonicotinic acid hydrazide group.

Indications and Contraindications for Combined Chemotherapy in Tuberculosis

A Indications

I. Acute Forms

1. General miliary tuberculosis	Triple combination: streptomycin intramuscularly 1.0 daily, phthivazid 1.0-2.0 daily or tubazid 0.45-0.6 daily and P.A.S. 12.0 daily for 2 to 3 months, then for 1 to 2 years, but not less than a year, phthivazid and P.A.S. or tubazid and P.A.S. in the same dosage
2. Tuberculous meningitis	Ditto
3. Pulmonary miliary tuberculosis	Ditto
4. Gaseous pneumonia	Ditto

II. Chronic Forms of Pulmonary and Pleural Tuberculosis

1. Chronic hematogenous dissemination	Triple combination: tubazid or phthivazid+streptomycin+P.A.S. for 2 to 3 months, then double: tubazid or phthivazid+P.A.S.
2. Nodular or infiltrative pulmonary tuberculosis	Initially, double or triple combination, later two drugs: tubazid or phthivazid+P.A.S. from 1 to 2 years. At lung decay—not less than 1.5 to 2 years
3. Fibrocavernous tuberculosis	Two or three drugs in indicated cases coupled with collapse therapy or surgery
4. Tuberculoma	Brief course of INH+P.A.S. At decay—lung resection under cover of chemotherapy
5. Pleurisy with effusion	Double combination: tubazid 0.45-0.6 or phthivazid 1.0 daily+streptomycin 1.0 intramuscularly for 2 months, then phthivazid or tubazid+P.A.S. If ineffective, hormone therapy coupled with synthetic drugs—ACTH or prednisolone for 1 month. Chemotherapy for not less than a year

III. Extrapulmonary Tuberculosis

1. Tuberculosis of the respiratory tracts (larynx and bronchi)	Streptomycin intramuscularly+P.A.S. or streptomycin+phthivazid. Continuously Aerosol with streptomycin or saluzid
2 Tuberculosis of the alimentary organs	Streptomycin+phthivazid Vitamins of the B-group. Polyvitamins
3. Urogenital tuberculosis	Streptomycin+phthivazid or P.A.S Continuously
4 Bone-and-joint tuberculosis	Streptomycin+phthivazid, phthivazid+P.A.S. Continuously
5 Skin tuberculosis	Ditto

IV. Collapse Treatment and Surgery

1. Artificial pneumothorax	Before induction, chemotherapy for 2-4 months and then continuously together with artificial pneumothorax
2. Lung resection	Prior to intervention within 2-4 months; postoperatively, continuously, not less than a year
3. Extrapleural pneumothorax and thoracoplasty	Brief chemotherapy preoperatively and continuous (not less than a year) postoperatively

Note: At bacterial resistance to primary drugs, combinations are used with secondary drugs

B. Contraindications

1. Irremediable drug intolerance, drug fever, hemorrhagic syndromes, dermatites, stomatopharyngites, neurites and other symptoms when irremovable by hormone therapy (ACTH) and antihistamine drugs
2. Leukopenia and granulopenia
3 Hypertension and angiospastic symptoms, functional insufficiency of the kidneys
4 Marked disturbances on the part of *n. stato-acustici*. Stable vestibular disorders and auditory trouble (after streptomycin)

It should be noted that mycoses (skin lesions) sensitise patients and require caution in chemotherapeutic prescription and administration (preliminary desensitation by special treatment)

Chemotherapy may be continued for up to two years, its duration depending on the type of primary lesion and the time which has elapsed since the onset of pulmonary disease, as well as the incidence of destruction and metastases in other organs.

Criteria of efficiency:

1. Cessation of bacillarity (checked by cultivation).
2. Cessation of toxicemia, with a return to normal temperature and blood picture (hemogram and E.S.R.).
3. Resorption of pathologic changes in the lungs, cicatrization or stabilisation in the form of small residual changes, usually not producing relapses, confirmed by both general radiography and tomography.

Chemotherapy is discontinued 2 to 3 months after repeated clinical and radiological examination show progressive reduction of organic

changes. In destructive or generalised forms, more prolonged treatment is recommended. In practice, chemotherapy is conducted in alternating cycles. After a 2 to 3 months' course of streptomycin and phthivazid or a triple combination including P.A.S., a continuous course of phthivazid+P.A.S. is undertaken. Experience shows that in benign cases intermittent streptomycin therapy may be adopted, the drug being administered after 48 hours or twice a week with daily introduction of the secondary drug, mainly P.A.S. Intermittent therapy, however, is applied comparatively seldom, an uninterrupted course being more reliable.

It is especially important to commence therapy promptly, if possible before the onset of disintegration, which definitely brings the best results. Therapeutic effects mostly become apparent in the first 2-3 months of treatment. After varying periods of antibacterial therapy, the tubercle bacilli may develop varying degrees of drug-resistance. As stated earlier, the use of these drugs in combination with secondary drugs delays the development of resistance to the basic drugs which, however, depends on the correctness of administration. Irregular therapy in short courses or interrupted for various reasons by the patient himself, assists the development of drug-resistance. Combined chemotherapy is essential from the start, monotherapy being applied only in cases of intolerance to secondary drugs.

In choosing the drugs to be used one should remember D. L. Romanovsky's statement made in 1891 on the essence of chemotherapy. In his view, its significance lay in its specific effect on the pathogen, in the neutralisation of microbial toxins and the stimulation of the host-body's defence powers, the healing process as a whole being commanded, so to speak, by the organism; chemotherapy, according to Romanovsky, had the effect of liberating the defence powers, which under intoxication cannot be fully utilised.

Thus, apart from the bacteriostatic effects of the drugs, an essential factor in chemotherapy is the resistance of the human body.

CHEMOTHERAPEUTIC SIDE EFFECTS AND THEIR REMOVAL

Along with the therapeutic benefits of the drugs described, undesirable side effects occasionally arise. The therapeutic side effects are usually not pronounced and rapidly disappear with the discontinuation of chemotherapy and the adoption of adequate supportive measures. With larger doses of phthivazid or tubazid (isoniazid), nausea, vertigo, pains in the abdomen, and nervous hypersensitivity frequently appear. In some cases it is even found necessary to abandon chemotherapy.

On a number of occasions, these symptoms are of a toxico-allergic nature, resulting from certain features of the isonicotinic acid hydrazide metabolism. At times, there is an increase in the secretion of *a*-ketone acids, particularly pyridoxine (vitamin B_6). Administration of pyridoxine in such cases eliminates the side effects. They may often

be avoided by strict observance of dosages and adequate management of chemotherapy in general, taking into account early manifestations of side effects and promptly applying measures leading to desensitation.

Since chemotherapeutic drugs are usually administered not separately but in combinations, it is sometimes difficult to distinguish the effects of one drug from another. The author personally has mostly observed the development of allergic reactions manifested by urticaria-like or measles-like rash, maculopapular skin lesions, and sharply manifest dermatitis accompanied by persistent itching. Usually, these symptoms develop during or after the second or third week. Sometimes, although very seldom, there are severe hemorrhagic syndromes of the type of capillary toxicosis, arising, apparently, after administration of isonicotinic acid hydrazides.

In instances of streptomycin-intolerance, one should keep in mind the possible appearance of vestibular disorders, vertigo and headache with a more or less pronounced syndrome of motile instability; occasionally, vomiting occurs at changes of posture. When using dihydrostreptomycin, special note should be taken of the condition of the auditory organs and the possibility of deafness in certain cases as a result of damage to the VIII pair of cranial nerves (*n.stato-acusticus, n.cochlearis*). Hence, audiometry should be resorted to when prescribing dihydrostreptomycin and canamycin.

The use of phthivazid is followed by euphoria, somnolence and, in case of cardiovascular diseases like hypertension, pains in the cardiac area. Side effects are eliminated by terminating chemotherapy. If that should prove insufficient, antihistamine drugs, e.g., dimedrol (*Dimedroli* 0.02 to 0.05 g twice daily) should be prescribed. It is also useful to prescribe calcium salts, either in a solution (*Sol. Calcii chlorati* 10.0:200.0, one tablespoonful three or four times a day), or in the form of a gluconate (*Calcii gluconici* 1.0 three times a day). In severer cases, when every minute counts, hormone therapy (ACTH intramuscularly, 10 to 20 units twice daily) should be prescribed immediately.

Occasionally, it is possible to continue chemotherapy under cover of hormone administration. An essential factor here is an abundance of vitamins in the diet. When prescribing vitamins for prophylactic and therapeutic purposes during chemotherapy, the physician should:

1. Ensure a supply of ascorbic acid (0.25 to 0.35 g twice a day, for adults);

2 When using streptomycin, apply pantothenic acid (calcium pantothenate)—a member of the B_2 vitamin group in 2 issues daily, total dose 400 mg, particularly to preclude the toxic effects of the antibiotic on *n. stato-acusticus;*

3. In conducting chemotherapy with isonicotinic acid hydrazides, remember the usefulness of pyridoxine (vitamin B_6) injected intramuscularly in ampules of 50 mg 1 or 2 times a day or 0.025 2-3 times a day orally, to remove side effects.

CHEMOTHERAPY COMBINED WITH STEROID HORMONES (ACTH AND CORTISONE)

In a number of cases even continuous combined chemotherapy fails to produce a complete clinical effect. The cause may lie both in the character of the body reaction and in the nature of the organic lesions. Massive sclerotic changes, caseous necrosis, focal incapsulation, organised cavities, often prove refractory in conventional chemotherapy.

Experimental and clinical observations have shown that chemotherapy accompanied by the administration of certain hormones may alter the course in cases of pronounced inflammation. As is commonly known, the steroid hormones of the adrenal cortex are able to induce rapid metabolic changes. This also applies to the adrenocorticotropic hormone (ACTH) now widely employed, which influences metabolism by stimulating the adrenal cortex. ACTH, a polypeptide, is secreted in the basophil cells of the frontal lobe of the pituitary. The purified drug is manufactured from the pituitaries of swine and cattle. It readily dissolves in water at a pH of 3 to 3.5. ACTH is delivered both dry and in bottled solutions containing 20 to 30 units, one unit being equivalent in its effect to the minimum quantity of ACTH which causes a 50 per cent weight reduction in the thymus of a four- to seven-day-old rat. The drug is injected intramuscularly, in doses of 10 to 20 units twice a day, always together with chemotherapy (streptomycin, phthivazid, P.A.S.). The drugs preclude the negative effects of the hormone on the tuberculous foci, the altered permeability of the tissues increasing the effects of antibacterial substances in the focal and perifocal area.

As an adrenocortical stimulant, ACTH causes corticosteroid hormones particularly glucocorticoids (corticosterone, hydrocortisone, cortisone, etc.), participating in the regulation of the protein and carbohydrate metabolism of fats and electrolytes, to be released into the blood.

Acting as powerful metabolic regulators, the adrenocortical hormones are controlled by the basic metabolic centres of the mid-brain, hypothalamus and pituitary. No effect can be expected from ACTH in the severest forms of pulmonary phthisis. It should be remembered that ACTH is prescribed only when the adrenocorticotropic function is unimpaired, which is determined by means of Thorn's test.

This test comprises of the intramuscular introduction of ACTH (25 units) with preliminary and subsequent eosinophil counts after Dunger at intervals of four hours With a positive test, i e , at least 50 per cent reduction of eosinophils, it may prove useful to prescribe hormones.

Continuous administration of ACTH may cause adrenohypertrophy. ACTH therapy is therefore continued for 1 to 2 months. Cortisone therapy, which is practised more rarely, may, to a certain degree, be regarded as a substitutory measure.

According to N. A. Shmelyov, the use of ACTH and, in certain cases, cortisone, is most obviously indicated in extensive infiltrative-pneumonic changes and caseous pneumonia. The author himself has obtained beneficial effects in recalcitrant cavities.

There have been indications of the favourable effect of ACTH in pleurisy with effusion owing to the reduced permeability of the connective tissue and capillaries (anti-inflammatory effect) (F. V. Shebanov). There is also evidence of the benefits of hormone therapy in tuberculous meningites.

We should like to emphasise once again the extremely beneficial effect of ACTH in the various forms of intolerance arising in chemotherapy. When applied together with hormone treatment, chemotherapy may be continued much longer.

However, hormones should be prescribed and chosen with caution, preliminary assays of the adrenocortical function being absolutely necessary. It is essential to account for the possibility of undesirable effects like arterial pressure drops and even, in rare cases, collapse.

Apart from the conventional ACTH, a longer acting drug called ACTH-zincum phosphate, is now available, a single injection of which is equivalent to 3 to 4 injections of ACTH (M. D. Moshkovsky).

Prednisolone (delta-I-hydrocortisone) and cortisone (11-dihydro-17-oxi-corticosterone-21-acetate) should be used with considerably greater discretion on roughly the same indication as for ACTH, e g., pleurisy with effusion. Occasionally, the drug may cause exacerbations. Cortisone for intramuscular administration is available in bottles containing 25 mg of the drug per ml; daily dose—from 25 to 100 mg.

Prednisolone is available in pills of 5 mg which is equal to 25 mg of cortisone.

PHTHIVAZID PROPHYLAXIS

Clinical experience in chemotherapy, as well as extensive experimental research, have lately brought up the problem of chemoprophylaxis as distinct from the specific prophylaxis now conducted with BCG. A conference held at the Tuberculosis Institute of the U.S.S.R. Academy of Medical Sciences approved a programme of such preventive chemotherapy, to be restricted to people living with bacillary patients, especially tuberculin-positive children, and to be conducted in the form of brief (2 to 3 months) courses with the use of phthivazid.

CHAPTER XIV

ARTIFICIAL PNEUMOTHORAX AND PNEUMOPERITONEUM

Artificial pneumothorax was first proposed in 1882 by Forlanini. In 1912, in Russia, A. N. Rubel and almost simultaneously A. Y. Sternberg assisted in the wide practical application of this method.

Essentially, artificial pneumothorax is purposed to provide the most advantageous conditions for the development of reparative processes in the tuberculous lung. Clinical experience has shown that the induction of artificial pneumothorax, i.e., the introduction of air into the pleural cavity, causes, first, a restriction of respiratory excursions, hence ensuring relaxation of the lung, and secondly, reduces the tension (expansion) of the pneumoparenchyma. The resultant selective pulmonary collapse is accompanied by lymphostasis. In such circumstances, the dissemination of microbes is, to a certain extent, hindered, while the development of connective tissue is encouraged. There is in the collapsed lung an increased propensity to reparative processes, the morphology of the inflammatory process being altered in such a way that the exudative phenomena give way to productive signs, cicatricial changes being especially conspicuous at the site of the lesion and in the perifocal area. With the reversible structural changes occurring in the lung during and after artificial pneumothorax, it is occasionally possible to achieve decisive results which alter the picture of the local tuberculous lesion. The resorption of exudative foci is accompanied by the collapse and closure of otherwise refractory tuberculous cavities. Especially favourable results are obtained by artificial pneumothorax combined with chemotherapy. It must be noted that after a two or three years' course of artificial pneumothorax has been concluded, the unafflicted lung areas may resume their normal function. Protraction of artificial pneumothorax for up to 4 or 5 years often leads to a loss of pneumoparenchymal elasticity and pleural thickening (rigid pneumothorax).

The reversibility of the changes caused by lung collapse in the unaffected sections is one of the essential features of this therapeutic method.

The results of treatment by artificial pneumothorax, which has been used for over 70 years, should be regarded as extremely significant. It may be claimed that with correct management pneumothorax led

to beneficial results with clinical recovery and rehabilitation in more than half of all cases. Some authors rate the results of pneumothorax still higher, claiming 60 to 70 per cent success.

Now, when chemotherapy is one of the principal methods of antituberculosis treatment, the indication for artificial pneumothorax are more restricted. However, Soviet clinicists, in contrast to their colleagues abroad, feel that artificial pneumothorax still retains its value, though with some reservations due to the achievements of antibacterial therapy. The phthisiotherapeutist should be fully equipped practically and theoretically for the use of artificial pneumothorax.

CONTEMPORARY INDICATIONS AND CONTRAINDICATIONS FOR ARTIFICIAL PNEUMOTHORAX

Unilateral artificial pneumothorax is prescribed in active and progressive forms provided that prognosis for other methods of treatment, primarily, chemotherapy, cannot be considered favourable, as e.g., in certain cases of cavernous tuberculosis, when the use of chemotherapy has not been sufficiently effective. Artificial pneumothorax is best induced at the stage when the febrile condition has been eased by preliminary chemotherapy and inflammatory processes in the lung have been restricted. Nor is its use altogether excluded in the febrile period (e.g., at hemoptysis). Artificial pneumothorax may be induced in the primary forms of tuberculosis, but is mostly applied in the secondary period.

Artificial pneumothorax is *indicated:*

1. In more or less fresh cases of an infiltrative nature with manifestations of disintegration determined radiologically, stethacoustically, or even only microscopically (*Mycobacterium tuberculosis* and elastic fibres in the sputum), not amenable to previous chemotherapy;
2. In limited dissemination with disintegration;
3. In cavernous lesions without marked concomitant cirrhosis;
4. As an emergency measure in hemoptysis and pulmonary hemorrhage, if the source has been established.

The field of application of bilateral artificial pneumothorax, which is quite feasible physiologically, has considerably narrowed since the advent of new chemotherapeutic methods. In cases of exacerbation in a contralateral lung during the management of unilateral artificial pneumothorax, the complication may be successfully arrested by combined treatment with chemotherapeutic drugs.

When considering the advisability of artificial pneumothorax, it is necessary to reckon with the presence of functionally efficient pneumoparenchyma in each individual case. It should be remembered that bilateral pneumothorax results in a lower degree of collapse than is true of unilateral pneumothorax, and the gas is absorbed somewhat sooner.

Artificial pneumothorax is *contraindicated*:

1. In widespread fibrocavernous and cirrhotic lesions with marked symptoms of thoracic deformity and particularly various manifestations of cardiovascular insufficiency of different origin;
2. With subpleurally localised cavities;
3. In acute caseous pneumonia and acute dissemination;
4. In tuberculous generalisation and metastases in other organs (intestine, kidneys, severe progressive lesions of the larynx, ulcerous lesions of the bronchi);
5. In cachexia.

In certain cases, the use of artificial pneumothorax proves possible after previous chemotherapy has reduced the pathological changes but has not brought about recovery, merely creating favourable conditions for possible pulmonary collapse.

APPARATUS, METHOD AND PROCEDURE IN ARTIFICIAL PNEUMOTHORAX

Treatment in artificial pneumothorax consists, basically, of the formation of an intrapleural air sac by means of a needle used to puncture the thoracic wall and introduce gas into the pleural cavity. In this way a closed pneumothorax is obtained. The basic distinguishing feature of a closed pneumothorax is the possibility of graduating its size within a broad range. Gas is induced into the pleural cavity by means of a comparatively simple device based on the principle of communicating vessels. High pressure in the system is obtained by pumping air with a Richardson syringe (Kondorsky's modification, sanatorium Visokiye Gori), or by raising to a certain height the cylindrical vessel included in the device, as in the models of Kachkachev and Heifetz. In all these devices, initial aspiration is ensured by the elastic traction of the lung. The devices may be used not only for inducing gas into the pleural space, but also for removing it, for instance, when spontaneous pneumothorax develops.

A special platinum needle, which is sterilised in the flame of a spirit burner prior to application, is most commonly employed.

The device should be sterilised at least once a month, the communicating vessels being half-filled with a 2.5 per cent solution of carbolic acid. Other equipment required is a hydraulic manometer and removable Sternberg-type cotton-wool filters for mechanical cleansing of the air introduced into the pleural space (Fig. 67).

PRIMARY INDUCTION AND MANAGEMENT

Artificial pneumothorax is preferably induced in a carefully sterilised operating room. In cases when movement is contraindicated, e.g., in hemoptysis, pneumothorax may be induced in bed, also with antiseptic precautions. Primary induction is usually carried out institutionally. We prescribe a 0.02 powder of *Codeini phosphorici* 30 minutes to 1 hour before induction.

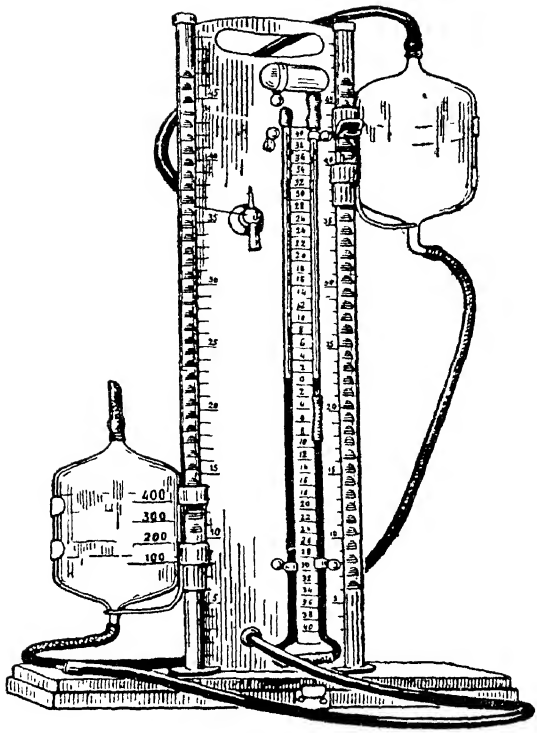


Fig. 67. Apparatus for inducing artificial pneumothorax (general view of modification manufactured at Krasnogvardeets Plant)

The patient is placed on a couch or operating table. The primary puncture is usually made along the mid-axillary line. The patient lies on his healthy side propped up by a side-rest to expand the intercostal spaces in the operating area. Patients with a labile, movable mediastinum may be operated in a supine position. The operating field is selected beyond the area of focal destruction, which is determined radiologically with all due precision. The puncture site is anointed with iodine. The puncture should be made without undue haste, the needle being swiftly passed through the skin and more cautiously through the remaining thoracic strata until the pleura is felt to have been punctured, the manometer beginning to indicate negative oscillations. If the oscillations are emphatic (e.g., from −12 to − 7mm) the pleural space is connected by turning the tap of the air-containing cylinder. Initially, the air is carefully induced by natural aspiration, and then under slight pressure, until 200 to 300 cubic centimetres are introduced, the manometer readings being checked after every 50 to 100 cubic cm.

Such uncomplicated primary induction is possible only with a free

pleural space. In more complicated cases special methods and more accurate orienting are required (Table 2). It is never advisable to induce a single ml of gas if the meter readings are obscure or vague. This is a basic guarantee against complications, primarily air embolism which occasionally, though rarely, may arise.

At the first filling, 200 to 300 ml of air are induced. On the second day this dose is repeated, subsequent refills being made every 2 or 3 days, then, finally, depending on individual circumstances, after a week, 10 days, and so forth.

As a general rule, artificial pneumothorax is carried out under negative pressure. When the air sac has attained optimum size, the pneumothorax should be maintained in such a way as to keep the sac at constant size.

COMPLICATIONS AT INDUCTION AND MANAGEMENT

Complications in artificial pneumothorax occur both at primary induction and during the subsequent period, i.e., they may be early or delayed. The symptoms may be: (1) pain, occasionally persisting after the removal of the needle at the end of insufflation, (2) traumatic pneumothorax owing to lung puncture; (3) subcutaneous and mediastinal emphysema; (4) air embolism; (5) pleurisy with effusion; (6) impaired collapse and re-expansion; (7) functional disorders on the part of the respiratory and circulatory organs.

A sensation of pain continuing after puncture may issue from the parietal pleura owing to exfoliation of the lung by the air sac in case of adhesive pleurisy. The affliction usually disappears swiftly. Two or three administrations of codein in doses of 0.02 are usually sufficient to alleviate the pain.

At times, pain arises when the air sac is unproportionately big in comparison with the volume of air induced. The development of an unproportionally big air sac is not always linked with spontaneous pneumothorax, sometimes depending on individual features of lung contractility (F. A. Mikhailov et al.). Painful sensations may be due to irritation of the parietal pleura during the actual puncture or to trauma inflicted on the tissues by the needle. Irritation of adhesions expanding at induction may also be accompanied by pain and occasional spasmodic rises in temperature. Traumatic pneumothorax with lung puncture, but without rupture, often brings no complications, but in certain cases leads to vulgar infection of the pleura and severe complications involving purulent and later mixed pleurisy.

Thanks to modern methods of induction under negative pressure, limited subcutaneous emphysema occurs increasingly rarely. This complication is mostly observed after compression pneumothorax, i.e., with positive pressure in the pleural cavity, due to which the gas may penetrate through the puncture channel into the subcutaneous cellular tissue. Not infrequently, it occurs in pleuroscopy, which is carried out at zero pressure. The symptoms of such complications

Manometer Readings[1] at Primary

Condition of pleural space and needle position	Manometer readings	Pressure variations at respiration
Pleural space free	Considerable negative pressure, e g , —14, —8	Free
Partial pleural adhesions	Marked variations, but below 1, e g , —1, —0 5,—0 5—0	More restricted
Extensive surface adhesions	Manometer silent	Absent
Needle end in lung (bronchus)	Pendulum-like oscillations ranging from —2 to +2	At arrest of respiration, immediate pressure drop at level of inhalation
Needle end in pleural cavity	Slight	Slight variations of negative pressure
Needle clogged	Often, no oscillations at all, or negligible oscillations after which manometer is silent	A rise after needle is cleansed with mandrin
Needle in blood vessel	Oscillations gradually increasing towards positive	Absent
Needle in abdominal cavity	Slight, about zero; positive at inhalation, negative at exhalation	Slight paradoxic
Needle in free pleural space. Lung emphysematous	Negative, e g., —2 —20	Considerable

[1] The difference between the level of liquid in the manometer bends is noted or else

Table 2

Pneumothorax Induction and Refills

Pressure rises during induction	Subjective sensations and objective disturbances	Note
Smooth, gradual	No special complaints after induction of 300-400 ml	Refill next day
More rapid increase, esp with small pleural pocket At expansion of adhesions — first swift rise, then drop in pressure	At induction, sensation of pressure or transient pain	With no pain, refill next day, if otherwise, a day later
—	Pain, cough, hemoptysis at lung lesion	One puncture at a time Repeated attempts only at new site
—	Pressure and pain	Immediately remove needle
At induction of moderate volumes of gas, rapid rise of positive pressure. Subcutaneous emphysema	—	Advisable to remove needle and make further puncture at later date, with sufficient skill, carefully advance needle, after which on clear-cut manometer indications, induce gas
Depending on conditions noted in §§ 1 and 2	—	Clean needle with mandrin
Do not induce!	Occasional pain	Very dangerous! Immediately withdraw needle
—	Occasional pain	Withdraw needle
—	Occasional complaints of obstructed breathing	Tactics decided following period of observation

the rise from zero in one bend is doubled.

can usually be removed by applying a pressure bandage, followed by several days of complete rest. Mediastinal emphysema is a severe complication, accompanied by inordinate swelling of the subcutaneous tissue on the neck and face. The condition is marked by deglutitive disorders and hoarseness; in certain cases the prognosis becomes grave. Such complications are extremely rare. To avoid the development of subcutaneous and mediastinal emphysemata, care must be taken not to shift the needle from side to side during puncture, or to allow considerable positive pressures in the pleural cavity. At the appearance of emphysema, a pressure bandage should be applied along with codein to alleviate cough and, in cases of considerable coughing irritation, pantopon or morphine is to be injected subcutaneously in doses of 0.01 g.

Such a severe complication as air embolism is now comparatively rare, mostly being observed not during primary induction but during refills.

The author has witnessed a case when during a two-years course of artificial pneumothorax, the patient sneezed and immediately fell unconscious, which was followed by vomiting and the emergence of what is known as marble or cadaveral skin, terminating in death from cerebral lesion Autopsy revealed that death was caused by air embolism apparently arising at the rupture of an adhesion occasioned by an abrupt rise of pleural pressure during sneezing

In a summary of literature on the subject, N. S. Morozovsky and G. A. Lvovich point out that air embolism developed in 0.03 to 0 1 per cent of cases in which induction was carried out. Heaton, analysing the findings of a number of authors, states that 3,726 inductions of artificial pneumothorax were followed by 1.1 per cent of cases with menacing symptoms and 0 2 per cent of deaths, while in 69,176 punctures the proportion was 0.1 and 0.02 per cent respectively. With strict observance of surgical technique, air embolism occurs extremely rarely.

Air embolism develops abruptly, sometimes after a sharp coughing impulse or change of posture. The ensuing symptoms are skin pallor, often vomiting and convulsions. The pupils cease to react to light, and the patient becomes unconscious. Marble or cadaveral skin is a frequent symptom. In benignly terminating cases such conditions continue for several minutes and in severe cases for several hours. In one case the author observed in 1916, the patient recovered consciousness on the following day, pareses disappearing 3 or 4 days later.

In some of the severer cases death follows immediately, in others, after a time. The basic means of preventing embolism are impeccable technique and careful preoperative treatment. At the onset of embolism, the patient is put in the Trendelenburg position, and camphar oil and coffein—rarely adrenalin—are applied; if respiratory motility is intact, the patient is given oxygen; otherwise, artificial respiration is employed.

COMPENSATION OF ARTIFICIAL PNEUMOTHORAX

(Pleuroscopy and Cauterisation of Adhesions)

On occasions when, owing to string-like and strand-like adhesions, the position of the air sac does not permit necessary collapse, the measure of choice is thoracoscopy or, more correctly, pleuroscopy. With the help of a thoracoscope, the condition of the pleural membranes and the nature of occuring adhesions are investigated. If tubercles are found on the pleura, intervention is ceased.

In its Soviet modifications, the thoracoscope provides a sufficient field of vision, which permits good observation of the pleural adhesions. As a rule, all adhesions found to hinder collapse are subject to cauterisation (Figs. 68, 69). This operation, proposed in 1912 by

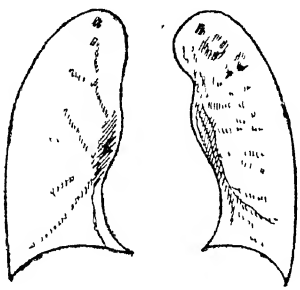


Fig. 68. Infiltration with cavity in superior section of left lung

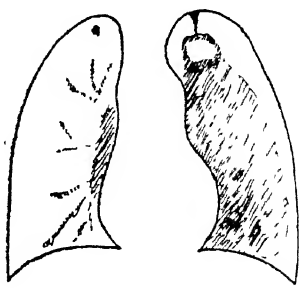


Fig. 69. Strand-like adhesion hindering lung collapse

Jacobaeus, has been further developed in Soviet clinical practice. The danger involved is insignificant. According to N. G. Stoiko (1938), out of 1,672 cases of pleuroscopy, cauterisation of adhesions gave positive results, i.e., collapse, in 1,051. Thus, effective outcomes were observed in 67.1 per cent of cases. The operation is frequently followed by the development of pneumopleurisies, which usually soon resolve. After the successful destruction of adhesions, the resulting lung collapse and artificial pneumothorax give a benign effect. The continuing presence of adhesions promotes the development of pleurisies. In such cases, therefore, pleurocautery is an essential preventive measure.

TECHNIQUE OF PLEUROSCOPY

The patient is prepared for operation by periodic refills Just before the moment of operation, the pressure in the pleural cavity should be reduced to zero (at expiration) When this is not achieved the abdomen is bandaged for the period of operation (F. A. Mikhailov, R E Kogan), which elevates the diaphragmic cupola and raises pleural pressure

After operation, the bandage is gradually released.

Prior to operation, the patient is placed on his healthy side which is supported by a side-rest The entire axillary area as well as part of the posterior and anterior surfaces of the thorax are treated with alcohol and iodine The site for introducing the thoracoscope is determined by radiography and radioscopy When the site has been selected, the area is anesthetised with a 0 5 per cent solution of novocain in the following order skin, intercostal muscles (each stratum successively), parietal pleura. On completing anesthesia, a small incision up to 1 cm long is made on the skin, into which the end of the trocar is inserted and gradually, without jerks, pressed into the pleural cavity The stylet is then replaced with the thoracoscope, by means of which the nature of the adhesions is ascertained, as well as their location in regard to the major vessels, the presence of tubercles, and all other features pertaining to the pleural cavity and lung proper The cautery trocar is inserted 1 or 2 intercostal spaces higher than the thoracoscope

The cautery should be kept at dark-red heat. The greater the heat, the less chance there is for tissue coagulation and the greater the risk of hemorrhage upon cautery Cauterisation should always be made at the thoracic end of the adhesion, nearer to the thoracic wall. Adhesions accessible from all sides should be cauterised, the shorter ones being severed only if they are more than 1 cm long, or else tissue coagulation may spread to the adjoining lung area and give rise to subsequent spontaneous pneumothorax.

MAINTENANCE AND ABANDONMENT OF ARTIFICIAL PNEUMOTHORAX

At present, under continuous chemotherapy, artificial pneumothorax may be kept up for $1^1/_2$ to 2 years. In future, the time of lung collapse is likely to be reduced still further. As it is, however, 18 months to 2 years are considered enough for the development of reparative processes and the collapse and closure of cavities.

The decision to abandon pneumothorax is taken after assessing the therapeutic effects by thorough clinical examination. Pneumothorax is best discontinued in winter and summer, but not in spring or autumn.

In order that the air sac should dissolve gradually, the volume of gas induced during refills is diminished, the actual number and frequency of refills being reduced. Re-expansion is assisted by temporarily retaining a small air layer, which, in case of favourable clinical findings (negative sputum, normal temperature, hemogram and E.S.R.) and a good general condition, is followed by complete cessation of artificial pneumothorax.

While artificial pneumothorax is abandoned, we recommend a course of sanatorium treatment and combined chemotherapy (phthivazid with P.A.S.) if the latter was discontinued at the start of re-expansion. Positive physical and rehabilitation tests showing good compensation (satisfactory functional tests after graduated exercise, e g., an hour's walk) mean that the treatment can be regarded successful and the results achieved favourable. During re-expansion patients usually resume work. If, however, at the start of re-expansion the patient was not allowed to return to habitual work—on specific clinical indications or for some other reason—there is no reason for forbidding such resumption after artificial pneumothorax has been terminated, if its results were favourable. For prophylactic purposes,

two-year follow-up is recommended, with appropriate adjustment of working conditions and recreation.

Artificial pneumothorax must on no account be continued for more than 2 years. After this time it loses therapeutic value, the pleura undergoing shell-like transformation, resulting in lung rigor and preventing re-expansion despite active aspiration. Unduly prolonged pneumothorax is fraught with the danger of the development of pleural effusion during re-expansion and subsequent pleural empyema—one of the severest complications following poorly managed artificial pneumothorax, requiring grave surgical interventions such as decortication, pleurectomy and so forth.

The rehabilitation prognosis after artificial pneumothorax is sufficiently favourable (Table 3).

Table 3

Rehabilitation on Abandonment of Artificial Pneumothorax
(Data obtained from Moscow antituberculosis institutions — I G. Lembersky)

Pneumothorax	Number of patients	Rehabilitation					
		Effective		Partial		Null	
		Absol number	per cent	Absol. number	per cent	Absol number	per cent
Unilateral	673	372	55 3	160	23 8	76	11 3
Bilateral	195	51	26 1	65	33 3	60	30 8

As the table shows, the percentage of cases with effective rehabilitation was 79.1, complete rehabilitation occurring in 55.3 per cent. It is likewise necessary to note the epidemiological importance of timely pneumothorax: effective collapse of the afflicted lung results in early abacillarity.

ARTIFICIAL PNEUMOPERITONEUM

Over the last ten years artificial pneumoperitoneum, earlier employed only for intestinal tuberculosis, has been used in the treatment of tuberculous lungs.

Basically, the procedure comprises the creation of conditions similar to those in artificial pneumothorax. After induction of air or oxygen into the abdominal cavity, the air sacs, usually located subdiaphragmally, lead to elevation of the diaphragmic cupolas (limited collapse), ensuring relative rest for the lungs, which is important for the afflicted organs.

Neuroreflex effects also play a definite therapeutic role in pneumoperitoneum.

The favourable results of artificial pneumoperitoneum in a number of cases and its comparative simplicity allow it to be recommended

on definite indications, especially together with chemotherapy. More recently, however, after greater experience, its application has been restricted.

We consider that artificial pneumoperitoneum is warranted chiefly in cases of open hilar lesions (Fig. 70, *a* and *b*) and infiltrative lesions in the lower lobes, or cases of hemoptysis when other measures have proved ineffective.

The technique employed in pneumoperitoneum is simple The puncture, according to the tradition followed at paracentesis in the treatment of ascites, is mostly made to the left of the umbilicus, in the middle of the line connecting the latter and the *spina iliaca anterior superior*, with a needle of platinum or the type used for intramuscular injections. The needle is inserted obliquely (in relation to the skin), its bevelled tip pointing downwards to ensure its entry into the peritoneal cavity immediately on puncture The needle pierces the two layers of the aponeurosis and the peritoneum, when the latter is passed the patient experiences pain The pneumothorax apparatus should be in readiness for inducing air at a moderate positive pressure The air rapidly flows in as soon as the tip of the needle enters the peritoneal space If the needle does not enter the space, the gas flows slowly, causing subcutaneous emphysema Definite pressure fluctuations, usually positive, ranging from+6 to+10 begin only after the formation of a sufficiently large air sac.

At the first induction, only 300 to 400 ml of gas are introduced The following induction is usually made on the second or third day (400 to 600 ml), the third or the 6th or 7th (500 to 700 ml), and the fourth on the 10th to 15th (800 to 1,200 ml) The dates of subsequent refills and the volume of air induced are determined by radiological control and functional findings (presence or absence of dyspnea, tachycardia) under careful clinical observation.

Pneumoperitoneum is carried out institutionally and, with a favourable course, is maintained for 1 or 2 years. Chemotherapy here is also essential.

The formation of a pneumoperitoneum is followed by a reduction of lung capacity, decrease of elastic tension, lympho- and hemostasis Under the influence of these factors, as in pneumothorax, the foci undergo varying degrees of resorption which is occasionally accompanied by collapse and subsequent closure of cavities, although the reparative processes are not as obvious as in artificial pneumothorax

Some cases are complicated by effusion or the development of fibrinous bodies.

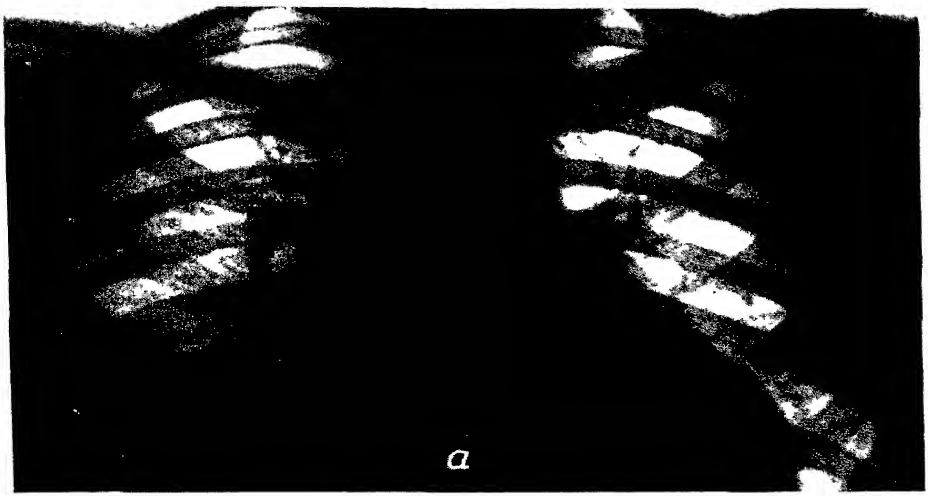


Fig 70a Big cavity in perihilar zone of right lung

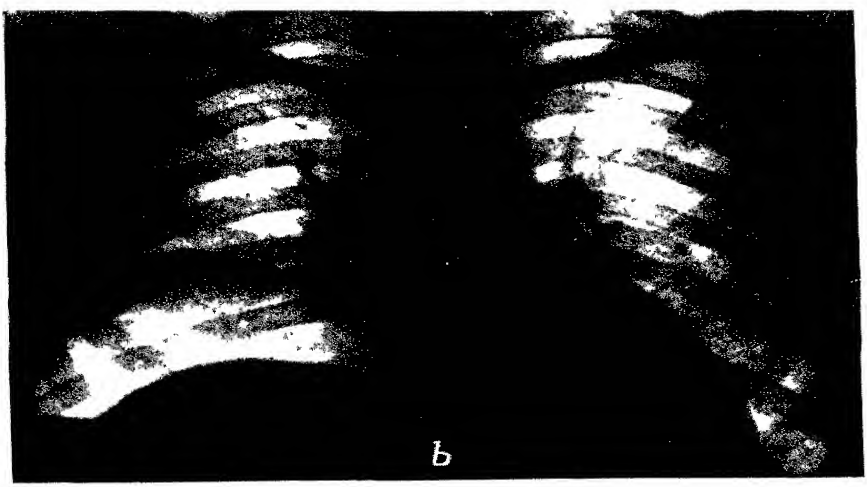


Fig 70b The same case after induction of artificial pneumoperitoneum

CHAPTER XV

SURGICAL TREATMENT OF PULMONARY TUBERCULOSIS

The use of surgical methods in the treatment of pulmonary tuberculosis began comparatively early. The beginning of surgical collapse therapy dates back to the early 20th century, the basic procedure being total extrapleural thoracoplasty. In the course of time this gave way to partial graduated apical thoracoplasty, which led to more limited collapse. In the last ten years, new methods of collapse therapy have been introduced, primarily the operation known as extrapleural pneumolysis. Experience has shown that, with a proper choice of cases, extrapleural pneumothorax and graduated apical thoracoplasty are quite suitable courses.

Apart from collapse therapy, in cases when pneumothorax proves either impossible or ineffective, radical surgery has been employed in recent years. The removal, on appropriate indications, of a lung destroyed by tuberculosis or limited lung resections in less extensive lesions, are the method of choice.

Thus, modern surgery of tuberculosis includes: (1) lung resection and (2) extrapleural thoracoplasty.

LUNG RESECTION

In recent years, due to the possibilities offered by modern antibacterial therapy, the spectacular development of anesthesia and the employment of intubation and inhalation narcosis under strict respiratory and circulatory control, wide use is being made of radical surgery. Since resection of an entire lung represents an extreme intervention considerably reducing the functional reserves and limiting future rehabilitation, segmental and lobar resection have now become very popular with physicians. In the U.S.S.R., N. M. Amosov, L. K. Bogush, I. S. Kolesnikov et al. assisted in the development and practical implementation of sparing segmental surgery. Sparing surgery, segmental surgery in particular, has insignificant detrimental effects on the lung function and does not cause the deforming processes associated with extrapleural thoracoplasty. With modern technical means, this operation is apparently the most sparing and, with proper choice of cases, the most promising.

Of course, resection of an affected segment does not bring radical recovery from tuberculosis, which is a general disease of the entire organism. In addition, the removal of a single segment does not rule out the possibility of different residual changes in the lungs, at times indiscernable even tomographically. Under modern chemotherapy, such changes may assume the form of fibrous and fibrocavernous foci in other sections of the lungs. Hence, thorough preoperative study of the condition of both affected and healthy lungs is essential, tomography being indispensable.

It must be noted that the removal of the principal focus—the source of bacillarity—creates more favourable conditions for the healing of the pulmonary lesion. Therefore, in a number of cases, especially when other methods of treatment prove invalid, segmental resection should be chosen. This refers primarily to the so-called tuberculoma and caseoma—circular fibrous-caseous foci with or without disintegration.

Modern indications for segmental resection include:

1. Lung tuberculoma, especially with symptoms of disintegration;
2. Rigid tuberculous cavities unamenable to other methods of treatment; bronchiectatic cavities and giant cavities restricted to a single lobe;
3. Residual cavernous lesions remaining after ineffective antibacterial or collapse therapy, i.e., refractory cavities in pneumothorax;
4. Bronchial lesions (stenosis of a lobar bronchus) with atelectasis and tuberculous lesions of the lung;
5. Repeated pulmonary hemorrhage (as an emergency measure).

The basic indication for pneumonectomy, i.e., resection of an entire lung, is a destroyed lung containing a system of cavities with bronchiectatic metastases, the contralateral lung being unimpaired. With these indications and careful clinico-physiological assessment of the functional reserves, lung resection generally produces favourable results.

Pulmonary surgery is conducted throughout under individually prescribed chemotherapy both pre- and postoperatively. The following clinical examples may serve as illustrations.

1. Patient M., female, age 36. Heredity and development normal. Had measles in childhood and cystitis at 17. Contracted tuberculosis 15 years ago. In 1939, revealed focal tuberculosis of the right lung, sputum negative. In 1941—infiltrative attack with disintegration in the right lung. In the same year, revealed infiltrative tuberculosis with disintegration in the left lung. From 1941 to 1947, treated by artificial pneumothorax induced in the right lung, which proved ineffective and was abandoned Late in 1948, revealed infiltrative-ulcerous tuberculosis of the larynx. Treated in Moscow City Tuberculosis Institute with streptomycin (35 g). Discharged after clinical recovery. In 1949, relapse of laryngeal process successfully treated locally by streptomycin (5 g). After 1948 had annual exacerbations In 1948, hemoptysis Annual institutional treatment with antibiotics gave temporary effects (altogether, received 90 g streptomycin and 35 g phthivazid). Admitted to Moscow City Tuberculosis Institute June 21, 1945. Operated for destroyed left lung. Diagnosis· chronic fibrocavernous pulmonary tuberculosis with dissemination (destroyed left lung). BK+EF+

On admission, general status unsatisfactory. Complained of agonising cough with expectoration (up to 100 ml), general weakness, subfebrile temperature. Impaired

percussion sound was noted in the upper lobe of the left lung. Stethacoustically, moist rales of different calibre along with harsh breathing in anterior part of upper lobe and the entire range of rales from different calibre moist to large-sized sonorous posteriorly, up to the IX rib Radiography and tomography showed destruction of the left lung (Fig 71, *a* and *b*) Blood picture (June 24, 1954) Hb 60 per cent; leukocytes 10,000; basophils 1 per cent; eosinophils 7 per cent, band cells 1 per cent, segmented cells 69 per cent; lymphocytes 16 per cent; monocytes 6 per cent; E.S.R 30 mm per hour. Sputum revealed tubercle bacilli and elastic fibres

Functional examination satisfactory pulse 98 per minute, breathing 18 per minute, Sabrazés' test 21 seconds, Stange's—39 seconds. Vital lung capacity 1,900 ml. Electrocardiogram normal. General supportive preoperative treatment (hygienic and dietary measures, blood transfusion). Streptomycin introduced intratracheally due to marked tracheobronchitic symptoms.

On July 27, 1954, total resection of left lung postero-laterally performed with separate treatment of hilar components Local anesthesia used in combination with alcohol-pentothal intravenous narcosis. Postoperative period without complications. Postoperative treatment included daily intrapleural injections of streptomycin (0 25 g) and penicillin (300,000 u) for two weeks; beginning with the third week, antibiotics administered every other day. Intrapleural administration of antibiotics accompanied by intramuscular injections (altogether, 34 5 g of streptomycin were introduced postoperatively).

Two months after operation the general condition was satisfactory. Patient could walk, cough ceased. Temperature normal. Dyspnea only when climbing stairs and walking briskly. Weight gained Blood picture: Hb 63 per cent, leukocytes 7,200, eosinophils 7 per cent, band cells 5 per cent, segmented cells 50 per cent, lymphocytes 28 per cent, monocytes 10 per cent, E S.R. 26 mm per hour; sputum negative. Radiological findings shown in Fig. 71, *c*.

Functional findings tendency towards tachycardia—pulse 120 per minute, breathing 16 per minute, Sabrazés' test 14 seconds, Stange's—27 seconds Vital lung capacity—1,300 ml (September 21, 1954).

Diagnosis: fibrocavernous tuberculosis of the right lung, quiescent; condition after total resection of the left lung

Conclusion: pulmonectomy for destroyed left lung resulted in clinical recovery

2. Patient K. V, female, age 19. No family cases Contacts denied Weak child, had measles, scarlet fever, whooping-cough, scrofula Frequent quinsy and influenza. In 1956-1957 complained of poor general condition, easy fatigue. In June 1958, prophylactic examination revealed tuberculoma-type infiltration in the right lung Antibiotics had no result.

Condition on admission satisfactory. Pyknic constitution Temperature subfebrile. No catarrhal symptoms in lungs Heart tones clear, extrasystolia after 20-25 beats. Three tuberculomata with disintegration revealed radiographically in II segment of the right lung (Fig 72, *a* and *b*). Sputum negative

Due to ineffectiveness of conservative treatment in this form, after satisfactory functional tests, patient was prepared for operation.

On September 21, 1958, resection of II segment of the right lung Postoperative course smooth. Lung fully re-expanded (Fig. 72, *c*). Within a month after operation, partial recovery of diaphragmic motility. Intoxication completely disappeared, together with extrasystolia

Pre- and postoperative treatment included antibacterial therapy.

Conclusion· the cited observation illustrates advisability of resection in cases of non-resultant etiotropic therapy in tuberculosis

Resectional surgery is bringing increasingly successful results which depend on a number of circumstances, including correct indications, methods and technique of intervention. Whereas early postoperative lethality previously reached 13 or 15 per cent and more, at present, according to several authors, it has fallen to 5 per cent and even 2.33 per cent, as claimed by N. M. Amosov. Remote lethality

after segmental resection is at present 1 to 3 per cent and even less.

Functional results and rehabilitation after segmental resection are extremely positive. Rehabilitation follows in a high percentage of cases. It should be borne in mind, firstly, that this operation leads to the removal of the main source of infectious dissemination, and, secondly, involves extremely slight and easily removable strain on the cardiopulmonary system.

Figures on recovery vary broadly, ranging from 59.3 to 91 per cent and more.

The remote results of sparing resections in our experience (Moscow City Central Tuberculosis Hospital) are reflected in the following table:

Table 4

Remote Results of Subsegmental Lung Resections in Tuberculosis

Total No of operated cases	Clinical recovery	Progression	No information	Death
480	437	15	25	3
100 per cent	91 per cent	3 1 per cent	5 2 per cent	0 6 per cent

Understandably, recovery cannot be stated until proved by time (at least 3 years). In 1954, according to Z. A. Kiselyova, rehabilitation was observed in 68 per cent of cases. The figures available now are even more encouraging.

Other operations on the lungs, particularly drainage and open treatment of cavities—cavernotomy—are at present performed more rarely, owing to the frequent possibility of using better methods of intervention, viz., sparing segmental resections.

EXTRAPLEURAL COLLAPSE THERAPY

Extrapleural Pneumothorax

Of all the methods of extrapleural collapse therapy, extrapleural pneumolysis with subsequent pneumothorax is the most preferable and least traumatising, involving the least impairment of the functional reserves. The operation has a negligible effect on the vital capacity of the lungs and its fractions, the slight lung damage due to collapse being soon compensated. An extrapleural air sac is usually formed by exfoliation of the parietal pleura over the lung lesion. Pleural exfoliation is undertaken after resection of the III and IV or another rib through a posterior paravertebral skin incision. The parietal pleura is separated from the endothoracic fascia with extreme caution, using the blunt edge of the scalpel. Exfoliation leads to the formation of an extrapleural cavity. The exudate accumulating in the latter is removed by repeated aspirations, the cavity being periodi-

Fig 71a Infiltration with disintegration in I-II segments of right lung

Fig 71b X-rays of the same case *Extrapleural pneumothorax* in right lung

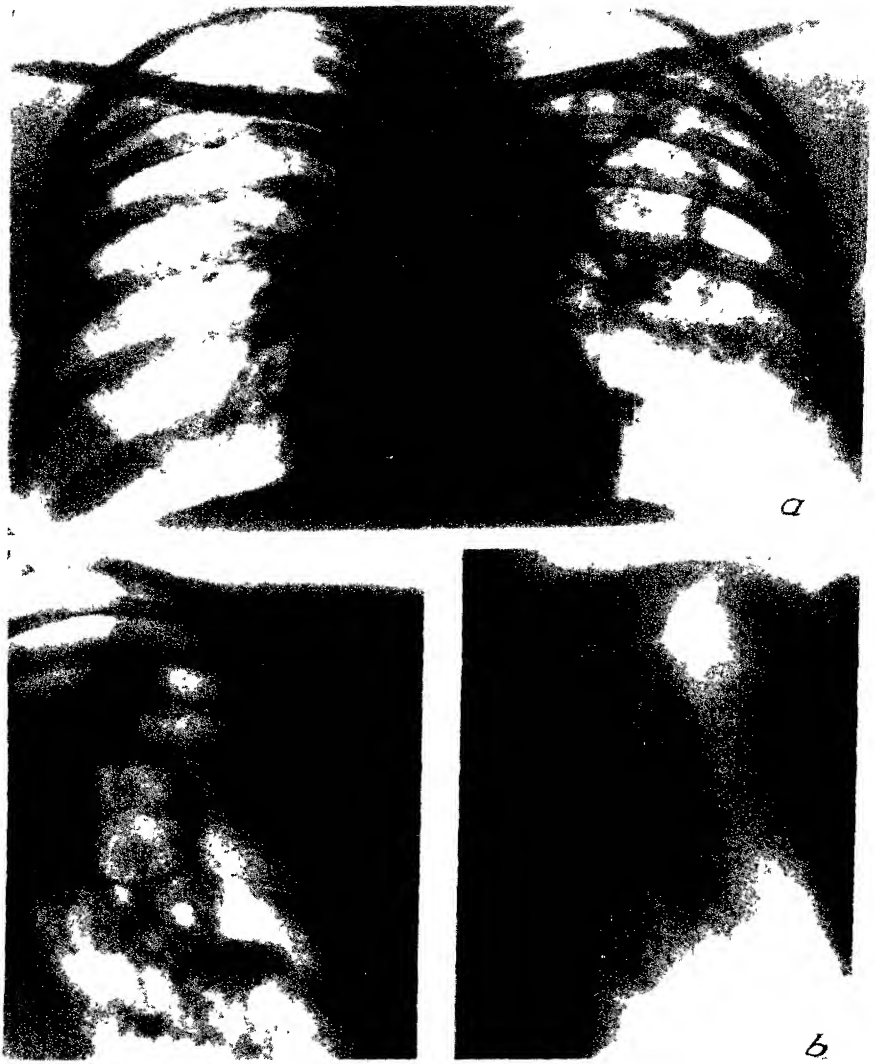


Fig. 72 X-rays of patient M
(a) chronic fibrocavernous pulmonary tuberculosis (destroyed left lung), *(b)* tomogram of left lung before operation.

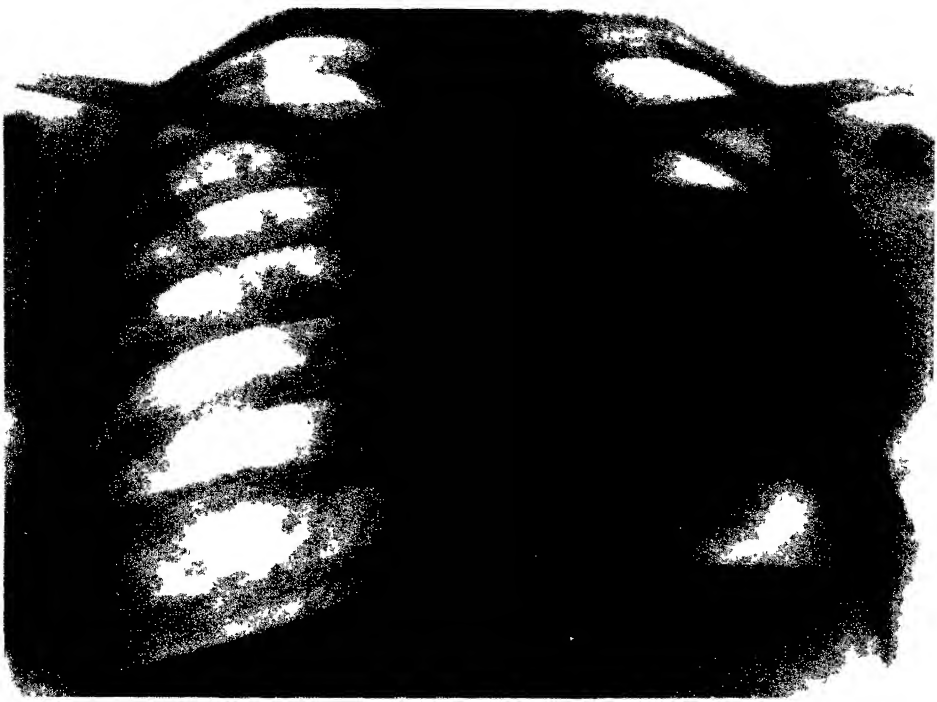
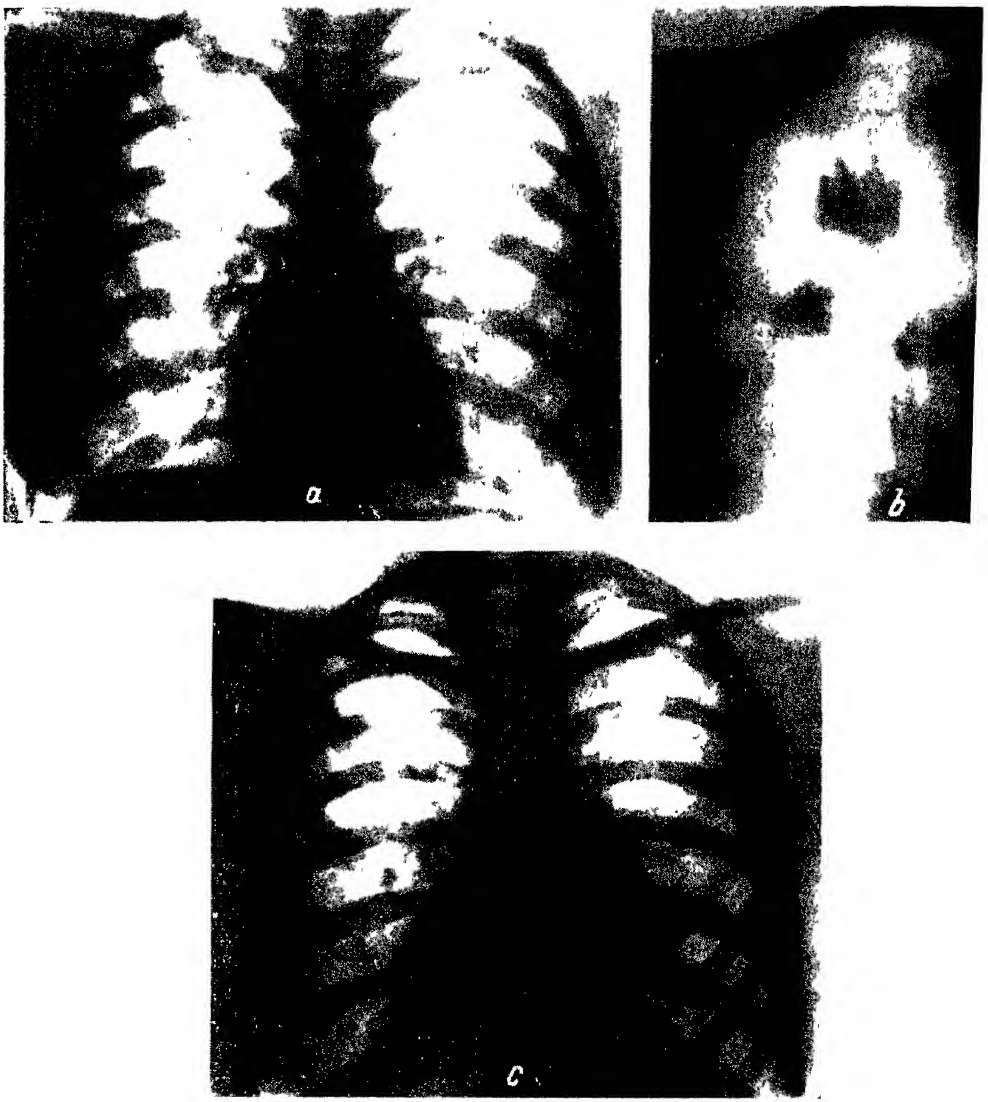


Fig 72c.
X-rays after operation—pulmonectomy


a
b
c

cally refilled with gas. With positive pressure, extrapleural pneumothorax is maintained for 2 to 3 years, depending on the extent of the original lesion (Fig. 73, *a* and *b*). In certain cases sterile vaseline oil (oleothorax) is used instead of gas.

Extrapleural pneumolysis, first carried out by Tuffier in 1891, has found wide application only in the last thirty years. In the U.S.S.R. N. G. Stoiko contributed much to the development and practical implementation of this valuable method. With correct management, re-expansion of the lung at cessation of refills is one of its main advantages.

On the basis of considerable clinical experience, extrapleural pneumothorax may be regarded as indicated in cases when classic intrapleural artificial pneumothorax proves unsuitable due to widespread surface adhesions. Extrapleural pneumothorax may be successfully induced in hemoptysis when an intrapleural pneumothorax cannot be applied. Extrapleural pneumolysis is used in limited and centrally located cavities, primarily in the upper lobes, whose collapse and closure cannot be effected by chemotherapy.

Extrapleural pneumothorax has highly beneficial therapeutic results, and, according to Russian authorities like T. N. Khrushchova, brings clinical recovery in 60 to 70 per cent of cases.

Extrapleural Thoracoplasty

Graduated apical extrapleural thoracoplasty has approximately the same field of application as extrapleural pneumothorax. It is used in cases when the presence of widespread pleural adhesions precludes the comparatively free exfoliation of the parietal pleura, and thoracoplasty with resection of the V-VII ribs appears more advantageous. Total thoracoplasty is at present applied comparatively rarely. Graduated apical thoracoplasty is carried out under local anesthesia The number and size of costal segments to be resected is determined by the nature and extent of the tuberculous lesion. Since thoracoplasty is followed by the development of irreversible changes such as thoracic deformities and contraction of collapsed lung segments, it is especially important to judge the condition of the contralateral lung and the functional reserves of the respiratory organs.

With a proper choice of cases, mostly including cavernous lesions with insignificant fibrosis, the remote results of extrapleural thoracoplasty are quite satisfactory, bringing recovery in 50 to 70 per cent of cases.

The operation is preferably performed in the non-febrile period of the disease. Both extrapleural pneumothorax and thoracoplasty are carried out under cover of combined chemotherapy· streptomycin and phthivazid in daily doses of 1 g and, subsequently, phthivazid and P A.S , 12 g daily.

DECORTICATION AND PLEURECTOMY

The physician often has to deal with a complication unamenable to conservative treatment and chemotherapy, viz., shell-like consolidation of the visceral and parietal pleura as a result of chronic tuberculous empyema. Often, such complications are connected with grave deformative changes of the pleura (pachypleuritis) and, occasionally, with a pleuropulmonary fistula. In these cases, when indicated, the operation known as decortication (removal of fibrous growth from parietal pleura) and pleurectomy (removal of the entire pleural sac) as well as resection of the afflicted segment, are the only means of relieving a severe ailment unamenable to conservative treatment and leading to amyloidosis. The mentioned operation may be called restorative, since after removal of the shell the function of the lung is partly restored. In the absence of massive cirrhosis, the lung re-expands on the operating table.

CHAPTER XVI

EMERGENCY MEASURES, SYMPTOMATIC TREATMENT AND TUBERCULIN THERAPY

Hemoptysis and Hemorrhage

Streaks or clots of blood in the sputum frequently occur in initial forms as well as in chronic fibrocavernous tuberculosis, cirrhoses and brochiectases, and congestion of the lesser circuit. Very often, grave complications do not ensue from these symptoms, but the appearance of blood streaks in the sputum is sometimes followed by hemoptysis or hemorrhage. Occasionally, lethal hemorrhage occurs when a major vessel is involved. If the patient is not helped in time, death may follow from asphyxia resulting from occlusion of the respiratory tract by coagulated blood.

Slight hemoptysis requires only physical and mental rest, viz., short-term bed-rest with administration of drugs containing bromide and calcium (to accelerate blood coagulation).

Rp Sol Natrii bromati ex 6 0×200 0
S. One tablespoonful 3 times a day
Rp. Sol Calcii chlorati 10 per cent–200.0
S One tablespoonful 3-4 times a day.
Rp Calcii gluconici 1.0
D t.d. N XX
S One powder 3 times a day.

In tending patients, special care must be paid to bed posture which should ensure free expectoration. It is important to allay the patient's fear of hemoptysis. Mental tranquillity is of extreme importance.

To achieve redistribution of the blood, i.e., to relieve the strain on the lesser circuit, tourniquets are applied for an hour to the lower extremities, accompanied by injections of *Ol. camphorae* 20 per cent, 2 g, and 500 to 600 ml oxygen subcutaneously.

In cases of more extensive hemoptysis which cannot be rapidly arrested, artificial pneumothorax in the affected lung or, in case of pleral obliteration, pneumoperitoneum should be applied. As a hemostatic measure, transfusion of blood of the same group is recommended (100 to 200 ml). Because of the danger of asphyxial pneumonia

narcotics fully suppressing the cough reflex (morphine, pantopon) are inadvisable. They should be given only in extreme cases, such as choking cough.

For the first two or three days the patient is given a limited amount of food in the form of liquids and gruel, as well as fruit and meat jellies. When expectoration of fresh red blood ceases, the diet may be somewhat more varied, to include milk porridge, grated soup, meat soufflé, soft-boiled eggs and apple purée. Ascorbic acid is added to the food in doses of 0.2 to 0.3 g 2 or 3 times a day. After blood-stained sputum disappears, the patient may be prescribed a normal varied diet. The food should be served warm, but not hot.

In cases when hemoptysis (cavital) continues and cannot be arrested by collapse therapy, surgical intervention is applied, viz., extrapleural pneumolysis or even resection of a cavitated lung segment or lobe. In some cases hemorrhage ceases without subsequent complications, but in others it leads to aspiratory pneumonia, which in the first days is treated the same as non-specific pneumonia. The measures employed include penicillin (600,000 u in two doses) and streptomycin (1,000,000 u). Cardiac activity is best maintained by camphor.

After the removal of complications, antituberculosis treatment is continued in accordance with the form and stage of the disease.

Spontaneous Pneumothorax

The treatment of spontaneous pneumothorax resulting from spontaneous or postoperative lung perforation (e.g., puncture by the pneumothorax needle), is accomplished depending on the type of pneumothorax in hand. If a closed pneumothorax is observed and the pleuropulmonary fistula does not function, temporising tactics are resorted to alongside with bed-rest.

In case of a pronounced defect of the pulmonary tissue and the emergence of a pneumothorax with positive pressure in the pleural space, causing edema and disturbances of cardiac activity, the gas is periodically evacuated by means of the pneumothorax device, reducing the pressure in the space to zero or even negative value. If this does not produce the desired effect and the patient's condition progressively deteriorates, permanent evacuation of the gas should be ensured by means of electric aspirators of the Titarenko type or a simple water-flow pump. Such aspiration is to be repeated. In case of failure, a thin catheter is introduced into the pleural space through a trocar, the catheter being connected to an aspirator for permanent (*a demeure*) aspiration to be kept up continuously (for 2 or 3 days). To ensure better obliteration of the pleural space, in a number of cases a solution of 5 drops of iodine tincture in 3 cubic ml of 40 per cent glucose is introduced into the space through a needle or draining.

In certain cases segmental or lobar resection has to be employed.

Symptomatic Therapy

Very often, tuberculosis patients are disturbed by cough. A useful way of easing coughing is the classic method of "coughing discipline" to which physicians often used to resort The patient is taught to endure the cough stimulation with equanimity, not to expectorate voluntarily, and to facilitate expectoration by drinking alkaline salts (e.g., borzhom) with an equal quantity of warm milk.

Among the drugs, which may be recommended the best results are obtained from codein.

Rp. Codeini phosphorici 0 015 (0 02)
Sacchari albi 0 3
Mfp D t d N X
S One powder 1 to 3 times a day.

If codein (0.015-0.02) is of no avail, dionine (0.015) is prescribed.

As regards the general symptoms evidenced in tuberculosis, i.e., toxicemia, the causal therapy applied at present includes: (1) antibiotics and (2) hygienic and dietary treatment (air therapy!). Fever and night sweats are usually amenable to such therapy, with the exception of extremely grave cases when drug treatment proves ineffective.

Personal hygiene in all its aspects is extremely important for the tuberculous patient. This particularly refers to the febrile period of the disease. Skin hygiene, sponging with water and eau-de-cologne relieve the patient's condition at this stage, permitting better rest.

Impairment of such vegetative functions as appetite and sleep is best treated by hygienic and dietary measures. Soporifics (bromural, medinal, adalin, etc.) should be prescribed only for more persistent disorders.

Tuberculin Therapy

Existing estimates of the effects of tuberculin on the tuberculous organism indicate that it should be regarded as an immunogenic agent. By means of repeated and continuous administration of tuberculin in progressively increasing doses, tuberculin resistance and, consequently, resistance to the metabolic products of tubercle bacilli are heightened, accompanied by various degrees of desensitation.

Tuberculin therapy may be applied only with a pronounced tuberculin skin reaction, under constant radiological control, as well as systematic control of the sputum, focal reactions (careful auscultation), blood (hemogram and E.S.R.), temperature and body weight. In certain cases, when there is almost no reparative tendency, stimulative tuberculin treatment under chemotherapy enhances the action of antibacterial drugs. Contraindications include all acute processes, extrapulmonary metastases and hemoptysis.

Tuberculin dilutions are prepared according to the following table.

Dilutions of Koch's Old Tuberculin (O. T.)

N. 1 0	Dilution	Content of pure tuberculin, mg	
		In entire 1-g syringe	In one graduation of 1-g syringe
0.	Pure O T.	1000	100
1.	1/10	100	10
2.	1/100	10	1
3	1/1000	1	1/10
4	1/10000	1/10	1/100
5.	1/100000	1/100	1/1000
6.	1/1000000	1/1000	1/10000
7.	1/10000000	1/10000	1/100000
8.	1/100000000	1/100000	1/1000000
9.	1/1000000000	1/1000000	1/10000000
10.	1/10000000000	1/10000000	1/100000000
11.	1/100000000000	1/100000000	1/1000000000

Treatment is usually begun with low dilutions. Injections are made every 4 to 5 days, the dosage increasing each time by one tenth of a ml of the given dilution. Any reaction (temperature) should be avoided, and in case of pronounced general reaction, especially focal, tuberculin therapy should be either abandoned or, with a slight reaction, returned to lower dosage after reactive symptoms have disappeared.

Treatment is usually continuous, covering several months, the course being varied according to individual features of the case in hand.

APPENDIX

Residual Changes Observed

Type of recovery	Functional status
1 Complete a) *restitutio ad integrum* b) limited sicatricial changes	No deviations from normal Wide adjustability
2 Residual changes without functional impairment	Deviations from normal absent of negligible, compensative reserves satisfactory
3. Pronounced residual changes with moderately reduced functional reserves	Degree of compensation dependent on nature of residual changes Limited adjustability
4 Metatuberculous syndromes	Markedly reduced functional reserves with labile nervous system. Poor adjustability
5. Recovery after surgery. a) conservative b) radical	1. Functional reserves unreduced 2 Functional reserves reduced

Note: 1 General requirement in all types of recovery—abacillarity
2 Absence of specific intoxication symptoms

at Clinical Recovery

	Clinico-radiological findings	Rehabilitation	Follow-up
	Practically, no residual pathological changes	Complete	Prophylactic and general
	1 Limited sclerosis and calcification Indurated areas 2 Limited residual local changes (incapsulated, indurated, calcified) 3 Pleural involvement	Complete	Periodic prophylactic examinations with X-ray control at dispensary for at least 2 years
	1 Fibrous and cirrhotic changes after focal and destructive lesions, including residual foci 2. Sclerosis with bronchiectases 3 Moderate emphysematous changes	Limited, to a varying degree	Dispensary follow-up for at least 3 years
	1 Diffuse pneumosclerosis 2 Pneumocirrhosis (bronchiectasis) 3 Fibrothorax 4. Concomitant emphysema 5 Different degrees of cardiopulmonary insufficiency	Drastically limited or absent	Systematic follow-up and treatment
	1 Without thoracic deformity and topographic disturbance of thoracic organs 2 With thoracic deformity, lung retraction, and displacement of mediastinal organs	Unlimited or moderately limited Limited to various degrees	Dispensary follow-up for at least 2 years Dispensary follow-up for at least 3 to 5 years

3 Absence of tuberculous extrapulmonary pathology
4. Postoperative residual changes delineated according to basic table (I-IV) of types of recovery

Drug-Resistance of Mycobacterium Tuberculosis
(γ/ml of medium)

	Phthiva-zid (tubazid)	Strepto-mycin	P A S	Ethio-namid	Cyclo-serine	Cana-mycin
VI Congress of phthisiatrists	More than 1	More than 5	10			
Central Tuberculosis Institute and Moscow Central Clinical Tuberculosis Hospital	1	10	10	10	10	10
Tuberculosis Institute, Ministry of Public Health, Russian Federation	More than 1	10	10			
Tuberculosis Institute, Leningrad	5	10				
Pasteur Institute (a) Rist (b) Kolletsos	 0.1-2 0 5	 2-4 5	 0 25-0 5 0 5	 10-20	 15-20 20	 10-15
International assay	0 2-1	4-8	1			
Czechoslovakia	0 2	10	0 25			
Poland	0 2	10				
F.R.G (Meissner)	0 1	4-8	0.5-1	5		

Note: 1. For INH drugs, the clinical limits of resistance in fast and slow INH inactivators differ, varying from 0 5 to 5 γ/ml Assays should be done as per tubazid and expressed in γ of tubazid.
2. Double values (Rist's data)—depending on the number of cultivated colonies
3 The wide variation of values for P A S. are, apparently, accounted for by the fact that we estimate P.A S resistance without recomputing for pure acid
4 In most foreign laboratories resistance is estimated with the use of the Löwenstein-Jensen medium, not less than 0 00001 mg and not more than 0 001 mg of mycobacteria used for cultivation

TO THE READER

Peace Publishers would be glad to have your opinion of the translation and the design of this book.

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